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Titel der Dissertation:

Causation or Assortative Mating: The Social Dynamics in Couples with Both  
Partners Suffering from the Same Lifestyle Disease. A Case Series Study from  
a German Cohort Study of Type 2 Diabetes Mellitus Patients in a Disease  
Management Programme

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*Für meine Eltern*

# 1 Introduction

## 1.1 CDRM main study

This dissertation is about the spouse with Type 2 Diabetes Mellitus (T2DM) as a risk factor for developing the disease oneself.

The study presented here is a spin-off of the industry sponsored CDRM Study:

Computer Based Diabetes Risk Management - Evaluation of an integrated care program for the support of secondary prevention and therapy of T2DM (CDRM-Studie: Computer gestütztes Diabetes Risiko Management – Evaluation eines integrierten Versorgungsansatzes zur Unterstützung der Sekundärprävention und Therapie des Diabetes mellitus.), for which ethical approval was obtained from the IRB of Philipps University Marburg on 28 August 2007.

The aim of the main study was to compare the impact of informing patients about their 10-year individual complication risk profile in the context of a disease management programme (DMP) according to SGB V §137f 1 on the incidence of specific T2DM complications in a cluster-randomized controlled clinical trial.

The study presented here has the title:

*Causation or Assortative Mating: The Social Dynamics in Couples with Both Partners Suffering from the Same Lifestyle Disease. A Case Series Study from a German Cohort Study of Type 2 Diabetes Mellitus Patients in a Disease Management Programme.*

Incidentally, it was observed that in the main cohort study, with  $n=398$  in the T2DM Disease Management Programme with the patients aged between 40 and 69, there was an unexpectedly high proportion of married couples in this disease management programme: of an overall  $n=398$  patients, there were 36 patients living in 18 marriages, seeing the same doctor.

In a strict sense, it cannot be tested, whether this proportion is higher than to be expected with random association, because the following parameters are unknown:

- The age distribution of married Type 2 Diabetes mellitus patients in the DMP in combination with the age distribution of their spouses/life partners
- Selectivity of T2DM couples within and outside of the T2DM-DMP, who are spouses/life partners of a T2DM patient. Such couples, for example, lead more disciplined lives and, therefore, may be more likely to be enrolled in disease management programmes. Such an effect, however, cannot be very strong, since approximately 2/3 of all known Type 2 Diabetes Mellitus patients in Germany are enrolled in a type 2 diabetes mellitus disease management programme. (Bundesversicherungsamt (Hrsg), 2015; Deutsche Diabetes-Hilfe, 2017)
- Selectivity of T2DM couples into the study: such couples, for example, may be more altruistic and, therefore, may be more likely to volunteer for participation in the study.
- Self selection of T2DM couples into one of the study medical practices: each of the identified 18 married couples went to the same study medical practice: not a single couple went to different doctors in the study. But note: we cannot observe T2DM couples, of which only one partner presents to one of the study medical practices.

Since the number of cases of married couples with T2DM was too small for typical sample-based evaluation, a case series study design had to be used. (For a detailed description and explanation see section 1.2.3.)

## 1.2 State of Knowledge

### 1.2.1 Type 2 Diabetes Mellitus

#### 1.2.1.1 Epidemiology

Diabetes mellitus is a group of heterogenic diseases with a chronic course. The common characteristic of all diabetes diseases is a hyperglycaemia. 90-95% of all Diabetes mellitus patients in Germany suffer from a Type 2 (peripheral insulin resistance) and less than 5% from a Type 1 (pancreatic insulin deficiency) Diabetes mellitus (Deutsche Diabetes-Hilfe, 2017). The remaining 5% come from other forms of diabetes mellitus, such as MODY (Maturity Onset Diabetes of the Young) or gestational Diabetes mellitus or rare diseases with secondary diabetes mellitus (e.g. haemochromatosis, cystic fibrosis and other) with varying pathogenesis. (Herold, 2018; Jameson *et al.*, 2018, pp. 2850–2853)

Diabetes mellitus Type 2 is one of the most frequent non-communicable diseases with ever increasing frequency, and one of the clinically most relevant complications of pandemic obesity. (World Health Organization, 2003; Segula, 2014)

Simultaneously obesity as the main risk factor of T2DM has increased in the past years as well. In more than 70 countries the prevalence of obesity has doubled within less than 30 years. (Afshin *et al.*, 2017)

Diabetes mellitus was the second leading cause of overweight-related deaths in 2015 just behind cardiovascular diseases. (Afshin *et al.*, 2017)

According to the International Diabetes Federation, in 2017, there were about 425 million people (20-79-year-olds) with Diabetes mellitus worldwide, most of whom are suffering from Type 2 Diabetes mellitus. This makes a worldwide prevalence of DM of 8.8% (also 20-79-year-olds. (Evans *et al.*, 2000; International Diabetes Federation, 2017, pp. 43–45)

According to the Global Burden of Disease Study approximately 475 million people from all ages were suffering from Diabetes mellitus (460 million from T2DM), which equals 6.4% of the worldwide population (6.28% for T2DM) with a large increase within the past years. In the year 2000 the prevalence has



been 4,68% for Diabetes mellitus (4,51% for T2DM). (Institute of Health Metrics and Evaluation - GBD Study, 2018b)

Diabetes mellitus is also one of the ten leading causes of death worldwide. (Institute of Health Metrics and Evaluation - GBD Study, 2018a)

There are numerous studies about the prevalence of Diabetes mellitus in Germany with conflicting results.

The DEGS1-Study shows a prevalence of Diabetes mellitus in Germany of 7.2% (in 18–79 year olds) with a rising prevalence at an increasing age (lifetime prevalence of over 20% in over 70 year olds). Furthermore, it shows a prevalence of an undiagnosed Diabetes mellitus disease of about 2%.

With 7.0% of the male and 7.4% of the female population, both sexes are similarly affected. (Heidemann *et al.*, 2013)

Other studies show a prevalence between 6.1–8.6% with increasing numbers from 2007 onwards. (Robert-Koch-Institut, 2015; Tamayo *et al.*, 2016, pp. 177–182)

According to the Global Burden of Disease Study the prevalence in Germany has risen from 7.2% in the year 2000 to 10.03% in the year 2017. (Institute of Health Metrics and Evaluation - GBD Study, 2018c)

A study about the prevalence development over the next years predicted an increase of 2.4 million people in 2010 to 3.9 million people with T2DM in the year 2030. (Brinks *et al.*, 2012, pp. 791–797)

Type 2 Diabetes mellitus is a disease with a strong increase in prevalence in older people. The prevalence in over 80-year-old adults (males and females) is over 23%, whereas the prevalence in 20–79-year-old adults is between 6–9%. (Tamayo *et al.*, 2016)

Another epidemiologic factor influencing the prevalence of the disease is social status, with a much higher prevalence in people with a low social status. (Connolly, 2000, pp. 173–177; Heidemann *et al.*, 2013)

These numbers in combination with the knowledge of complications and subsequent diseases, show what a widespread disease T2DM is and the

impact it has on the health of about 9-10% (diagnosed and undiagnosed) of the German population.

### **1.2.1.2 Pathophysiology and Genetics**

For a better understanding of the research question and the study design a brief explanation of the pathophysiology of Diabetes mellitus is crucial.

Describing the disease in a nutshell Zaccardi et al. used the following sentence:

‘Diabetes mellitus is a complex metabolic disorder associated with an increased risk of microvascular and macrovascular disease’. (Zaccardi *et al.*, 2016, pp. 63–69)

Type 2 Diabetes mellitus is a disease, which is characterized by an insulin secretion disorder as well as a reduced biological response to insulin leading to a decrease in glucose uptake by the target organs, including liver, skeletal muscle and white adipose tissue. From this follows a hyperglycaemia which again aggravates the disorder as exposure to excessive glucose levels is toxic to the beta-cells of the pancreas, thus creating a *circulus vitiosus*. (Lammert and Zeeb, 2014, pp. 164–166)

In contrast to Type 1 Diabetes mellitus the T2DM shows an increase of insulin secretion by the  $\beta$ -cells in the pancreas in the beginning of the disease as a mechanism of compensation for the insulin resistance in the peripheral tissues. (Lammert and Zeeb, 2014)

The cause of the disease is influenced by polygenetic factors with a complex interaction with modifiable exogenous factors. (Köppel, G; Kreipe, 2016)

The highly familial accumulation and the high concordance in twins suggest a genetic background in the pathophysiology of T2DM. The significant differences in the T2DM-frequency between different populations also suggests a genetic influence. The prevalence between different ethnic groups varies widely, from 1% in Chile Mapachu Indians, to 41% in the different ethnic groups of Nauru and about 50% among Pima Indians in Arizona. These differences can partly be explained by differing lifestyle factors, however the large differences in prevalence between ethnic groups with similar environments support the idea of

genetic influence to a predisposition of Type 2 Diabetes mellitus. (Das and Elbein, 2006; Jameson *et al.*, 2018, pp. 2850–59)

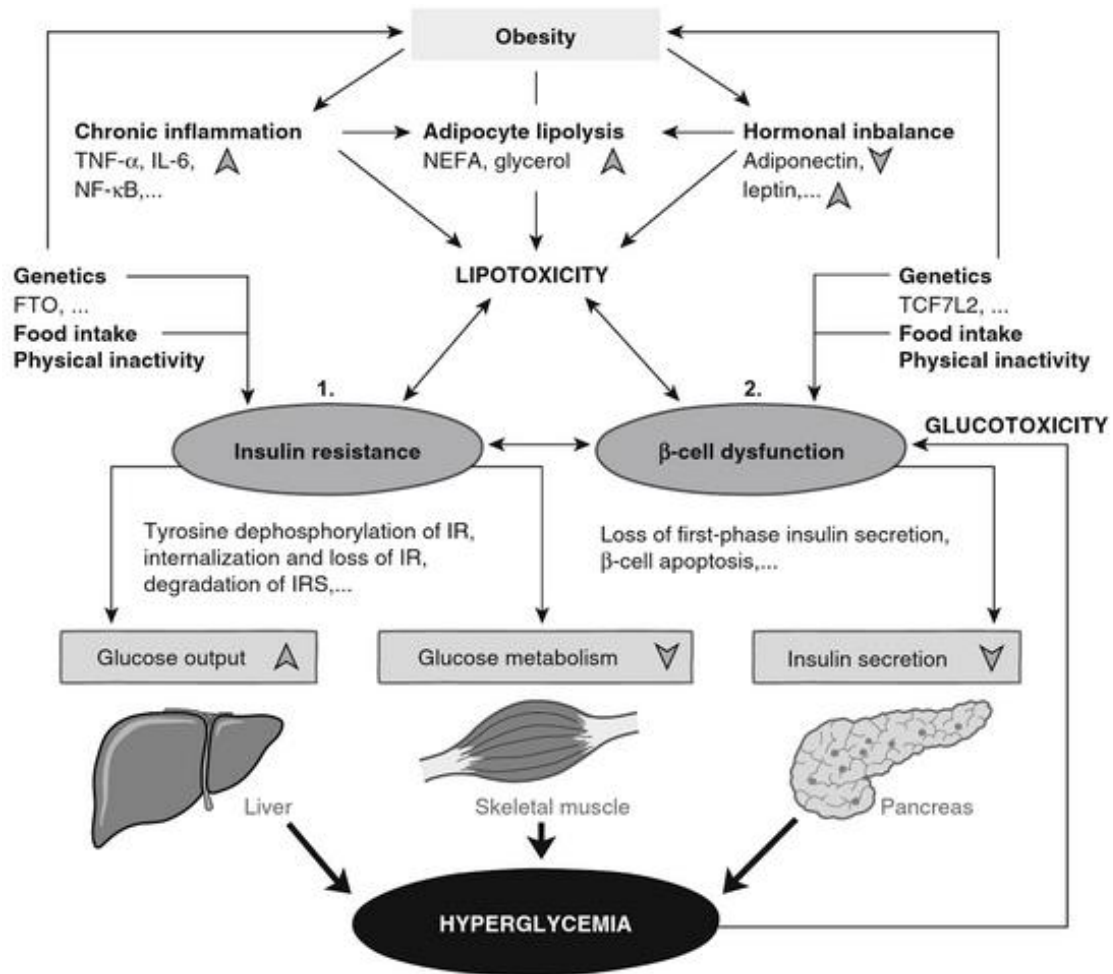
For more than 95% of the T2DM-patients, it remains unknown which genetic defects are inherited, how they are inherited and how they influence the pathological mechanism. The few genes that have been identified are inherited autosomal dominant and all of them had a negative impact on the insulin secretion. The patients with these genes suffer from a diabetes called MODY (maturity-onset diabetes of youth). (Jameson *et al.*, 2018, pp. 2856–2859)

The main exogenous factor is obesity and most (80% or more) T2DM patients are obese. (Jameson *et al.*, 2018, pp. 2856–2859)

Different studies have shown that especially the duration of obesity increases the risk of developing T2DM, independent of the degree of overweight and obesity. (Abdullah *et al.*, 2010; Reis *et al.*, 2013, pp. 1241–1247; Hu *et al.*, 2014, pp. 2267–2273)

The following figure shows the complex interaction between the different factors promoting the manifestation of T2DM:

**FIGURE 1** PATHOGENESIS OF TYPE 2 DIABETES MELLITUS (Lammert and Zeeb, 2014)



This figure summarizes the complex interaction between obesity, the pancreatic function and the peripheral tissues in T2DM.

As mentioned earlier, two major pathophysiologic characteristics contribute to the development of T2DM. These two characteristics are insulin resistance in the target organs and beta-cell dysfunction in the pancreas.

Adipocytes secrete factors that induce these characteristics, making obesity one of the major risk factors for developing T2DM.

In the beginning of the disease, the insulin resistance can be compensated by an increased pancreatic insulin secretion. Over time, glucose level increase and the inflammatory response of the adipose tissue intensifies. The so called

glucotoxicity and lipotoxicity lead to a further decrease in beta-cell function. (Lammert and Zeeb, 2014)

Also influencing the progress of insulin resistance and beta-cell dysfunction are genetic factors. Nevertheless, studies have shown that the modifiable risk factors of Type 2 Diabetes mellitus explain about 80% of the increase in world wide prevalence. (World Health Organization, 2018)

This means the exogenous modifiable factors, such as being overweight and obesity, play a bigger role in the increase of prevalence than the unchangeable factors. (Chan *et al.*, 1994, pp. 961–969; Schienkiewitz *et al.*, 2006, pp. 427–433)

With being overweight and obesity as the main risk factor for Type 2 Diabetes mellitus, it is clear that all lifestyle habits leading to being overweight and obesity, can be determined as risk factors as well. These include especially diet and physical inactivity. (World Health Organization, 2018)

### **Diet:**

Increased consumption of refined carbohydrates and saturated fat in combination with a lower intake of fruits and vegetables, leads to weight gain, thus increasing the risk of T2DM. (World Health Organization, 2018)

It has been shown that it is very likely that an increased consumption of sugar leads to higher Diabetes risk. (Schulze and Hauner, 2011, pp. 58–74)

### **Physical inactivity:**

The same risk applies for physical inactivity. The preventive effects of only 30 minutes of physical activity on five days per week was measured as a Relative Risk  $RR=0.7$ , as studies have shown. (World Health Organization, 2018)

Only by increasing physical activity the risk of developing T2DM can be decreased by up to 30%. (Orozco *et al.*, 2008)

But, on average, physical activity in rich societies has decreased drastically and the energy uptake has increased compared to earlier generations. (Schatz, 2014)

### **1.2.2 Spouses as a risk factor in other diseases**

To get an idea of the impact of a spouses' health status on one's own health it makes sense to look at studies observing this in different other diseases.

Apart from type 2 Diabetes mellitus, it has been detected in a variety of other diseases, that spouses with a certain disease seem to be a risk factor for that disease.

These other studies show a correlation of lifestyle factors in spouses as well as a correlation in diseases.

### **Life Style Factors**

A study made in the Chinese population called *Spousal Correlation for Lifestyle Factors and Selected Diseases in Chinese Couples*, observed spousal association in different lifestyle factors and selected diseases. The study included 66,130 married couples and came to the conclusion that a '[...] shared marital environment may contribute to similarities in lifestyle and morbidity in spouses'. Another observation from this study was that women were more likely to adapt habits (such as smoking or consumption of alcohol) from their partners than the other way around. (Jurj *et al.*, 2006, pp. 285–291)

A similar observation was made in the USA studying smoking behaviours in newly married couples. In that work, which is called *Spousal influence on smoking behaviors in a US community sample of newly married couples*, it has been detected that the influence of the male partner on his wife was larger than the influence of the female partner on her husband. (Homish and Leonard, 2005, pp. 2557–2567)

## **Chronic Kidney Disease**

Another study, including 95 spouses of 178 haemodialysis patients, showed that spouses were at an increased risk of developing a chronic kidney disorder (CDK) when the partner was a haemodialysis patient. The conclusion of this study was also that the spousal concordance suggests an important role of mutual health behaviours and environmental factors in developing a chronic kidney disease. (Tsai *et al.*, 2010, pp. 856–866)

## **Alcohol Dependence**

An additional idea on the reason for such a high concordance in so many different diseases has been brought up in the following study: *Spousal Concordance for Alcohol Dependence: Evidence for Assortative Mating or Spousal Interaction Effects?*.

In this study, 5,974 twins and 3,814 of their spouses were interviewed by telephone and it was observed whether assortative mating or spousal interaction led to an increased concordance of alcohol dependence. The conclusion was, that both assortative mating and spousal interaction may have contributed to the increased concordance of alcohol dependence in the couples. (Grant *et al.*, 2007, pp. 717–728)

There are many more sources in the research literature dealing with the topic of spouses as risk factors.

## **Major depressive episode (MDE)**

A study from Lindeman *et al.*, within the Finnish population, observed 1,708 male – female spouse pairs and major depressive episodes were assessed within the sample. Beside alcohol intoxication at least once a week and a chronic medical condition, a spouse's major depressive episode was a risk factor for a MDE. (Lindeman *et al.*, 2002)

## **Overall Health Risk Status**

This study observed spousal concordance health risk status and compliance among 9,620 opposite sex couples. The analysis showed a spousal concordance for both health risk status and compliance status. (Pai, Godboldo-Brooks and Edington, 2010)

## **Hypertension**

The study aim was to observe blood pressure levels within spouses and an assessment of a spouse as a risk factor for arterial hypertension in a 17 year prospective study.

Results showed a concordance of blood pressure levels in spouses, which was conditioned by sharing a common environment as well as marital assortment. (Dolgalev, IV; Brazovskaia, NG; Karpov, 2013)

These very interesting observations in different diseases lead to the assumption that there are potentially two main causes for an elevated risk of both partners suffering from the same disease:

- the spousal interaction - this includes a shared and similar environment and an adaption of lifestyle choices such as smoking.
- assortative mating - including similarities of spouses in the genes, the educational level and the socio-economic status: people select mates with similar characteristics. (Domingue *et al.*, 2014)

These observations and ideas will play a role in formulating and shaping hypotheses in this dissertation.

### **1.2.2.1 Other studies dealing with similar topics**

Research on several ethnic groups already exists that suggests that spouses with an already manifested T2DM elevate the risk of their partner developing T2DM as well.



- Hemminki K, Li X, Sundquist K, Sundquist J. Familial risks for type 2 diabetes in Sweden. *Diabetes Care*. 2010. Vol. 33/ No. 2: pp. 293–297.

This is a study observing the familial risks for T2DM of affected family members, also including spouses. The results suggest a familial clustering of diabetes due to environmental factors as well as a genetic basis. However, the study only looked at the number of hospitalized patients with T2DM, which means only rough ideas about the reasons of the familial clustering could be won.

- Di Castelnuovo A, Quacquarello G, Donati MB, de Gaetano G, Iacoviello L. Spousal concordance for major coronary risk factors: a systematic review and meta-analysis. *American Journal of Epidemiology*. January 2009. Vol.169/No.1: p. 1-8.

This study looked at the concordance for coronary risk factors within spouses. They took databases from MEDLINE, EMBASE and PubMed and studied 71 papers.

The results showed a strong correlation in smoking and the body mass index between the spouses.

- Leong A, Rahme E, Dasgupta K. Spousal diabetes as a diabetes risk factor: a systematic review and meta-analysis. *BMC Medicine*. January 2014. 12/12: p. 1-12.

This study has a similar objective as this dissertation as it looks at spousal diabetes as a risk factor. A total of 2,705 articles were yielded and analysed.

The results showed an increased risk in developing a T2DM when facing a spouse with T2DM of 26%. However, this study did not have the objective to analyse the reasons of the increased risk.

- Khan A, Lasker SS, Chowdhury TA. Are spouses of patients with type 2 diabetes at increased risk of developing diabetes? *Diabetes Care*. March 2003. Vol. 26/No. 3: pp. 710–712.

In this study, the objective was to see whether spouses with T2DM are at increased risk of developing T2DM themselves.

Spouses of Type 2 Diabetes mellitus patients were compared to spouses of nondiabetic subjects.

The results showed a significantly increased risk in glucose intolerance in partners of T2DM patients.

- Trejo-Arteaga JM, López-Carmona JM, Rodríguez-Moctezuma JR, Peralta-Pedrero ML, Escudero-Montero R, Gutiérrez Escolano MF. [Risk of glucose metabolism changes in spouses of Mexican patients with type 2 diabetes]. *Med Clin (Barc)*. November 2008. Vol. 131/No. 16: pp. 605–608.

Just as in the previous study the objective was to compare spouses of T2DM patients to spouses of nondiabetic patients. The study was performed in the Mexican population and compared 87 spouses of diabetics with 87 spouses of nondiabetics.

The results also showed a higher risk of a glucose intolerance in the spouses of diabetics.

- Sun J, Lu J, Wang W, Mu Y, Zhao J, Liu C, Chen L, Shi L, Li Q, Yang T, Yan L, Wan Q, Wu S, Liu Y, Wang G, Luo Z, Tang X, Chen G, Huo Y, Gao Z, Su Q, Ye Z, Wang Y, Qin G, Deng H, Yu X, Shen F, Chen L, Zhao L, Bi Y, Xu M, Xu Y, Dai M, Wang T, Zhang D, Lai S, Ning G; REACTION Study Group. Prevalence of Diabetes and Cardiometabolic Disorders in Spouses of Diabetic Individuals. *American Journal of Epidemiology*. September 2016 Vol.184/No. 5: pp. 400–409.

A higher risk of suffering from T2DM when the partner is affected has also be shown in this study observing couples in the Chinese population.

- de Visser KL, Landman GW, Kleefstra N, Meyboom-de Jong B, de Visser W, te Meerman GJ, Bilo HJ. Familial Aggregation between the 14th and 21st Century and Type 2 Diabetes Risk in an Isolated Dutch Population. *PLoS One*. July 2015. Vol.10/No.7.

This study was looking at how different degrees of interrelatedness influence the risk of developing T2DM. It also showed a higher risk in spouses.

So, in conclusion some of these studies, like this CDRM study, had a completely different objective and only found the increased number of spouses as an incidental observation. Some of them did have the objective of observing, if there is a higher risk for people with spouses suffering from T2DM. However, an investigation on what the reasons might be has not been carried out in any of these studies.

### **1.2.3 Case series**

As mentioned earlier, the number of cases of married couples with T2DM was too small for typical sample-based evaluation (details below), so that a case series study design had to be used.

#### **1.2.3.1 Definition and description**

A case series is defined as 'a collection of patients with common characteristics used to describe some clinical, pathophysiological, or operational aspect of a disease, treatment, or diagnostic procedure'. (Porta, 2014, p. 37)

It is an observational and descriptive study design, which looks at patients and their diseases retrospectively and in which no comparison group is involved. (Bhopal, 2009, p. 234)

Case series can be subdivided in clinical and population based case series.

A clinical case series is mostly a coherent set of cases of a disease, which comes from a defined group of healthcare professionals (or hospitals etc.), whereas a population based case series includes all cases of a group of patients seen by all clinicians in a geographically defined region. (Bhopal, 2009)

Given the fact, that all spouses from the CDRM study were drawn from a group of clinicians, this case series can be referred to as a clinical case series.

It is important to consider what a case series can be used for and which conclusions can be drawn from it, as well as where its limitations are.

## **Disadvantages**

The main limitation '[...] of a case series is its lack of a comparison (control) group' (Carey and Boden, 2003, pp. 1631–1634), which might make 'temporal associations between putative causes and effects [...] unclear'. (Grimes and Schulz, 2002, pp. 145–149)

In the case of this dissertation, however, these temporal associations between putative causes and their effect are exactly the objective of the observation. The little number of patients combined with the great amount of information available gives a good possibility to get deep insights on the temporal associations between the possible risk factor of a partner with T2DM and possible effect of developing the disease. As the big set of data also contains a huge number of T2DM patients, who are (very probably) currently not in a relationship with a T2DM patient, opens up the opportunity to generate a randomly selected control group. This means this weakness does not fully apply to this work.

Another weakness of a clinical case series, like this one, compared to a population based case series is, that the list of cases (spouses with T2DM) is very unlikely to be complete for this region, as not all clinicians from this area participated in the study. (Bhopal, 2009)

On the other hand, the information obtained from these clinicians are very detailed and give a deep insight into the medical history of the patients.

Case series do have the limitation of the atomistic fallacy. This is the assumption that observations made in individuals or small groups apply to an entire population. (Bhopal, 2009) This limitation can obviously not be ruled out.

## **Advantages**

As case series are usually observational studies they are very useful for describing 'disease characteristics related to person, place and time'. (Kooistra *et al.*, 2009, pp. 21–27)

This makes case series very valuable for shaping hypotheses: '[...] epidemiologists and clinicians generally use descriptive reports to search for clues of cause of disease—i.e., generation of hypotheses'. (Grimes and Schulz, 2002)

These case series (as well as other descriptive studies) are then often used as a foundation for larger studies with comparison groups. (Grimes and Schulz, 2002; Bhopal, 2009)

Another advantage is the low cost of the majority of descriptive studies as, in most cases the data is already available. (Kooistra *et al.*, 2009) In the case of this work, a significant amount of data was already available as the observation of a large number of couples was drawn from a previous study. Nevertheless, all of the patients were contacted again in order to maintain more information on each one.

In conclusion, it can be said that 'these studies offer some unique opportunities and perspectives on the pattern and causes of disease in populations, and provide a solid platform from which to explore the pathways to disease causation'. (Bhopal, 2009)

### **1.2.3.2 Examples of case series**

The possible value of case series can be seen in the following examples.

In December 1981 a case series was published in the *New England Journal of Medicine* with the title *Pneumocystis carinii pneumonia and mucosal candidiasis in previously healthy homosexual men*.

This case series was dealing with four cases of pneumocystis carinii infections in young homosexual men in Los Angeles, USA. (Gottlieb *et al.*, 1981)

These four cases turned out to be the first described patients suffering from HIV. (Merrill, 2015)

Following this case series, the disease was soon recognized in a variety of people including homosexuals, blood transfusion recipients, female sexual partners of men with AIDS and intravenous drug abusers. Two years after the observations made in the case series the human immunodeficiency virus (HIV) was isolated from a patient for the first time. (Jameson *et al.*, 2018, p. 1393)

HIV has since become a global pandemic with reported cases from all over the world. (Jameson *et al.*, 2018, pp. 1402–1404)

In 2012 AIDS was still the sixth most frequent cause of death world wide and in 2015 more than 33 million people in the world lived with HIV/AIDS. (WHO, 2014)

Another case study was made in 2001, where 11 cases of inhalational anthrax were diagnosed after bioterrorism. On the basis of this case series, which examined the patients thoroughly, a considerable amount of information was attained on the symptoms of anthrax, especially in view on how they differed with different kinds of exposure (inhalational and cutaneous). (Jernigan *et al.*, 2001, pp. 933–940; Jameson *et al.*, 2018, pp. 883; S2)

### 1.3 Derivation of the hypotheses

In this dissertation, it will be studied by which mechanism a spouse with a Type 2 Diabetes mellitus can become a risk factor for the partner to develop a Type 2 Diabetes mellitus herself or himself as well.

Summarizing the literature on the marriage partner with various non-communicable diseases as a risk factor for developing the disease oneself, such a phenomenon has been demonstrated to be more than a rarity. This consideration also makes the findings for T2DM couples even more reliable.

Since the number of cases of this study with 18 couples and 36 individuals is too small for any meaningful statistical testing, I cannot do more than assume from the literature mentioned earlier (see section 1.2) that such a non-random association between the T2DM risk for marriage partners exists in my study population, although I will remain unable to prove it.

Then the question arises, if this non-random association can be explained by assortment. It needs to be asked whether people with an increased disposition for T2DM have a more than random chance for entering a marriage, or if it can be explained by causality. Is it possible that people entered a marriage for other reasons than those that brought them the disease, but once they were married, the one who already had the disease or developed it later, subsequently infected the other one.

Before 1965, Sir Austin Bradford Hill developed nine criteria in order to distinguish in observational studies whether there are causal or non-causal associations in the genesis of a disease. Since then, these criteria often have been used, most notably in the well-known 1964 report, *Smoking and Health: Report of the Advisory Committee of the Surgeon General of the Public Health Service of the United States of America*. (Bayne-Jones *et al.*, 1964)

These criteria, which only refer to statistical associations, include: (Fedak *et al.*, 2015)

## Strength

Strong associations, in Hill's theory, are more likely to be causal for a disease than weak associations. Weak associations could supposedly be explained by undetected biases.

As an example for a strong association Hill refers to Percival Potts observation that the mortality of chimney sweeps from scrotal cancer was 200 times higher than of other occupational group, which lead to the correct conclusion that the exposure to tar and mineral oils was a risk factor for scrotal cancer.

Although that is a logical explanation there are counterexamples for strong association being causal and for weak associations not being causal for a disease.

For example, there is a weaker association between smoking and dying of cardiovascular disease although it is not doubted that smoking is an acknowledged risk factor for cardiovascular diseases. (Hill, 1965, pp. 295–300; Rothman, Greenland and Associate, 2014, pp. 24–27; Fedak *et al.*, 2015)

Referring to T2DM spouse as a risk factor:

The strength of the association has yet to be determined. The mentioned literature only gives us a vague idea on how strong the association between a spouse with T2DM and the developing of the disease is.

This data set is, as mentioned earlier, not large enough to state how strong associations might be.

## Consistency

Consistency means that an observation of an association can be made in different circumstances as well as in different populations. However, a lack of consistency does not prove that there is no causality between an observed factor and a disease. That is because causal factors do often need certain circumstances in order to be part of the causality. The



usage of a tampon for example can be a causal factor for a toxic shock syndrome, but only if other conditions, which might be unknown, are met. (Hill, 1965; Rothman, Greenland and Associate, 2014)

Referring to T2DM spouse as a risk factor:

Consistency can already be seen, as there are many studies with an incidental finding in different studies in different populations (see section 1.2).

## **Specificity**

The criterion of specificity has to be looked at with great care. According to Hill, specificity means that a cause has only one single effect. This assumption cannot be valid, as there are plenty of examples where one cause has multiple effects. A very common example is smoking as it shows causal association with lung cancer, cardiovascular diseases and several other diseases. (Hill, 1965; Rothman, Greenland and Associate, 2014; Fedak *et al.*, 2015)

Referring to T2DM spouse as a risk factor:

As already mentioned, this criterion has to be dealt with carefully and that is also the case here. It seems hardly possible to observe a factor and prove its specificity to one effect.

## **Temporality**

Temporality is a criterion which is inarguably necessary in order to show causality of a factor and a disease. Temporality means that a putative causal factor has to precede a putative effect. This, however, does not mean that a factor occurring after the effect can be ruled out as a potential cause in general. (Hill, 1965; Rothman, Greenland and Associate, 2014; Fedak *et al.*, 2015)

### Referring to T2DM spouse as a risk factor:

Temporality is one crucial criterion in the investigation of a causal association in spouses with T2DM.

Type 2 Diabetes mellitus is a disease which develops slowly with having risk factors over years. The high level of glucose does not create any symptoms in the first few years of the disease. Therefore, in order to suggest a causal association between being exposed to the putative risk factor there has to be a temporal association. This means one of the spouses has to suffer from T2DM for at least a few years, before the effect (partner also developing T2DM) sets in. (Wirth and Hans, 2013, pp. 184–186)

It is not possible to specify the exact amount of time of exposure to risk factors before developing Type 2 Diabetes Mellitus, but different studies have shown that the duration of exposure raises the risk. (Hill, 1965; Rothman, Greenland and Associate, 2014; Fedak *et al.*, 2015)

Taking into account these studies and the pathophysiology described earlier it can be said it takes at least two, but likely more, years of exposure to the putative risk factor (spouse with T2DM).

If this temporality cannot be seen in the observed spouses, a causal association can virtually be ruled out.

### **Biological gradient**

With his fifth criterion, which is the biological gradient, Hill states that a causal association is more likely when there is a linear dose-response curve. The example he uses to demonstrate this is the linear correlation between smoking and lung cancer. The probability of developing lung cancer rises linearly with the number of consumed cigarettes over the years, which suggests evidence for a causal association.

On the other hand, there are plenty of examples in medicine where there is a non-linear dose-response curve. In fact, in a minority of cases the curve is linear.

An example is the J-curved dose-response line in alcohol consumption, which shows a lower death rate in moderate alcohol consumers than in people who do not drink at all. The highest death rate, however, is seen in heavy drinkers.

There are also cases where a causal association comes along with a rapid increase in response. For example, the usage of diethylstilbestrol (DES) and adenocarcinoma of the vagina showed such a non-linear dose-response curve. (Hill, 1965; Rothman, Greenland and Associate, 2014; Fedak *et al.*, 2015)

#### Referring to T2DM spouse as a risk factor:

This criterion is not fully applicable to this example. The 'dose' cannot be perfectly measured in the risk factor 'spouse'.

The exposure, however, which can be measured would be the duration/amount of time spent together, which should be a topic in developing a questionnaire: A question could be included concerning when the couple started living together in order to find out how long a spouse has been 'exposed' to the other one.

### **Plausibility**

This criterion refers to the biological plausibility between the association of cause and effect. It assumes that if a statistical association between putative cause and effect can be observed, it has to be investigated from a state of biological knowledge.

Hill also understood that this point has to be put in perspective, as biological plausibility always depends on the scientific knowledge of the time. (Hill, 1965; Rothman, Greenland and Associate, 2014; Fedak *et al.*, 2015)

### **Coherence**

There is a very fine line between coherence and plausibility, which cannot be drawn perfectly.

What Hill means is that the causal association should not seriously conflict with either the natural history or the biology of the disease. He brings up the example of the histopathologic impact of smoking on the bronchial epithelium.

Nevertheless, current sources state that coherence and plausibility are not perfectly distinguishable in many cases. (Hill, 1965; Rothman, Greenland and Associate, 2014; Fedak *et al.*, 2015)

Referring to T2DM spouse as a risk factor:

Biological plausibility and coherence both have to be taken into account and investigated accurately. The already established biological associations should be pulled together with this epidemiological observation. This means that the already established risk factors (such as lack of physical exercise and obesity) have to be observed in the spouses.

## **Experimental evidence**

Experimental evidence means that an experiment might emphasize an assumed causal association. That means that in assumption of causal association an experiment is performed. If, in this experiment, a group of people are cut off from a potential risk factor, and it can then actually be observed that the disease does not occur, the likelihood of a causal association between the factor and a disease increases. (Hill, 1965; Rothman, Greenland and Associate, 2014; Fedak *et al.*, 2015)

Referring to T2DM spouse as a risk factor:

This criterion cannot be applied to this case, as a group of people could not be cut off from the risk factor, which is the spouse with T2DM.

## **Analogy**

Analogy might help in order to accept slighter evidence to see a causal association. Hill says, for example, that with the knowledge of the effects

of thalidomide and rubella in pregnant women, it would be easier to see a causal association of other drugs and viruses in pregnancy in the future.(Hill, 1965)

This criterion, however, interferes with the criterion of specificity as an analogy to cause and effect in other diseases rules out that a factor can only be causal for one effect.(Rothman, Greenland and Associate, 2014)

Also, critics say that with enough creativity, an analogy can be seen anywhere.(Fedak *et al.*, 2015)

#### Referring to T2DM spouse as a risk factor:

In this case, analogy is a very interesting criterion as there are many other studies where a causal association between patients with certain diseases and their spouses also developing this particular disease can be seen (see section 1.2. Spouses as risk factors for other diseases).

The hypotheses made in these studies should be observed and carefully taken account of in order to see possible analogies.

### **Research question**

In consideration of the Bradford Hill criteria, the following hypothesis can be formulated:

A person with T2DM is causal for the elevated risk of his or her spouse to develop T2DM as well.

### **Theoretical Example:**

In an imaginary controlled randomized trial:

There are two splits of populations: in one of them (Split A) of a total married population sample, people had to marry other people randomly; in the other split (Split B) people were allowed to marry whomever they wanted. We further have to assume that only a few people in the population suffer from T2DM.

In case only causality (T2DM patients infect their partners, but do not select them for their T2DM disposition) is true:

Number of T2DM patients is the same in split B as in split A;

Number of T2DM couples is the same in split B as in split A;

In case only assortment (T2DM patients do not infect their partners, but select them for their T2DM disposition) is true:

Number of T2DM patients is the same in split B as in split A;

Number of couples with T2DM is higher in split B than in split A;

To illustrate this, an oversimplified numerical example can be examined:

There are 10 men and 10 women with an initial disposition. If causality is given, these 20 people may infect their partners. In addition, there are 90 men and 90 women without the disposition, but they may be infected in the causality scenario. All infections have taken place within the first 10 years.

If only causality is given, but disposition is irrelevant for selecting a spouse, then after 10 years in split A as well as in split B there will be 19 T2DM couples (1 couple both with the disposition, 18 couples where one partner has infected the other, 81 couples without the disposition and without the disease) and 38 T2DM patients (the 20 with the disposition and 18 they have infected).

If only assortment is given, then after 10 years, in split A there will be 1 T2DM couple and in split B there will be 10 couples, and there will be 20 T2DM patients in both splits.

There are also other approaches to considering why there may be an elevated risk for developing T2DM for spouses of T2DM patients.

It is known that Type 2 Diabetes mellitus is more frequently seen in people with low socio-economic status due to increased risk factors such as obesity and lack of physical exercise. (World Health Organization, 2018)

It is also known, that people tend to find life partners with people of similar socio-economic status. This is called assortative mating. (Kalmijn, 1994, pp. 422–452)

Although assortative mating also includes genetic aspects, but as a study in the American population has shown, only about 10% of assortative mating can be explained by genetics. (Domingue *et al.*, 2014)

Therefore, people with a low socio-economic status are more likely to develop T2DM and are more likely to find a partner with an increased risk of developing T2DM.

These facts lead to another hypothesis:

T2DM patients lead to an increased risk for their partner to develop T2DM, because the partner is likely to share similar risk factors.

## **Research question**

### **Specific Study Population**

From the literature, it is known that a spouse with T2DM comes with a relative risk of approximately 1.3 – 1.4 for developing T2DM themselves. (Di Castelnuovo *et al.*, 2009, pp. 1–8; Hemminki *et al.*, 2010, pp. 293–297; Leong, Rahme and Dasgupta, 2014)

In this study, in both partners of the observed couples the T2DM disease had already manifested. Designs, in which initially healthy patients with and without a T2DM spouse are compared for a differential risk of developing T2DM themselves, are, therefore, not applicable.

The research question, therefore, is:

Can there be found informations in this present set of data, whether the slightly elevated relative ratio (RR) for T2DM in spouses of T2DM patients, which is described in the literature, could be explained by contagion (thus causal) or by assortative mating.

We have two kinds of data, leading to two kinds of data analysis approaches:

- A long list of clinical and lab parameters of all subjects from the study population (n=398). Of these, we know of 18 couples, that is 36 individuals;
- In addition, a list of behavioural and biographic parameters obtained from the complete interviews of 7 couples, that is 14 individuals.

## 2 Data and method

### 2.1 Identifying spouses in the data set

From the study population, we looked at patients with the same family names who belonged to the opposite sexes, who were a similar age and who had the same postal address. We identified 18 couples, that is 36 individuals, of which one couple were only identified by having the same postal address and were in the same age difference range as the other 17 couples, as their family name differed. We were not able to identify any same-sex couples – be it only by the same address – in the study population.

This will be a biased selection from all couples with two T2DM partners for the following reasons:

- It is not easy to observe married couples with different family names and different addresses, although such cases may be rare, especially in the age range of the study population (40–69 in 2009–2011).
- Two thirds of all known German T2DM patients are enrolled in a specific T2DM DMP, with socio-economic status, education, and health lifestyle as strong predictors of enrolment. Nevertheless, there may be a few couples seeing the same physician with only one partner being enrolled in the DMP.
- We cannot observe couples seeing different physicians, and they are not included in this study and we could not identify any couples seeing different physicians, who are taking part in this study.

The study physicians have their practices in the same region, but not in the same towns or cities. Therefore, in any case, the likelihood is that of couples seeing different physicians, one partner might have been seeing a physician who is not a study physician. This may be a major source of bias, as the decision of partners to see the same as opposed to a different physician may depend on different factors, such as duration of disease, co-morbidity, travel



time to work, size of town or city and other factors that may also influence the course of the disease.

Taking account of all these kinds of possible biases, it is likely that more than the already discovered 36 individuals in the study population are currently in a long-term relationship with another person also suffering from Type 2 diabetes mellitus.

The substantial bias, together with the small ( $n=18$ ) number of cases, leaves the option of a case-control study design for analysing the data according to (1) (see 1.3. Research question), although results have to be interpreted with great care.

In addition, all 18 couples identified in the main study sample, were invited to a telephone or a personal face-to-face interview, with the following outcomes:

- 3 couples could not be reached by one postal and 4 subsequent telephone invitations;
- 5 couples could be reached, but declined an interview for unspecified reasons;
- One couple had initially accepted but declined later;
- In one couple one partner had died shortly after the termination of the main study;
- In one couple, one had developed dementia, and the other declined for that reason.

The remaining 7 couples were interviewed as follows:

- 3 couples were interviewed face-to-face by this author, who for that reason travelled at two occasions to the recruitment area.
- In one couple, the husband had died from lung cancer three years before contact, but the surviving wife volunteered to answer on behalf of her deceased husband. Sufficient validity of the collected data can be shown through corroboration from the exit interviews of the large Health and Retirement study in the USA. (RAND, 2014)

The ideal proxy for exit interviews is a surviving spouse. Thus, it was decided to accept the offer that the wife answered for herself and – as proxy – for her deceased husband. She also was interviewed face-to-face by this author.

- 3 couples were interviewed by telephone by Dr Andrea Werdecker.

The substantial bias, together with the very small ( $n=7$ ) number of cases, means that the option of an informal case series design for analysing the data according to (2) is inevitable (see 1.3 Research question).

## **2.2 Interviews**

### **2.2.1 Data Collection and Approval by the Research Ethics Committee**

After conceiving the idea for this study, and after identifying the 18 couples as described above, an amendment application to the original application of the main study was submitted to the ethical review committee of the Medical School of Philipps University Marburg, which as of 21 January 2014 had no concerns about the planned study design (Reg. Nr. 92/07).

First, all married couples of patients in the CDRM study whom we could recognize as such were studied in the main study data set to see certain recurring patterns, which can at least show tendencies.

The next step was to see which information on the patients would be interesting and necessary, which the CDRM main study did not yet contain. This necessary information led to the idea of contacting all of the partnered patients again to set up an interview with them.

All interviewed couples were given full information on what kinds of questions they would be asked and what the questionnaire was for. They also signed an informed consent declaration.

### **2.2.2 Developing a list of topics**

As the patients to contact were a small group it was crucial to develop a questionnaire with questions precisely aiming at verifying or refuting the hypotheses.

So, the first task was to develop a list of topics, which had to be included in the questionnaire. These topics would have to contain the following points in order to be able to make a presumption about the causation of the spouses developing T2DM:

- The height and the weight at the beginning of the relationship in order to calculate the Body Mass Index (BMI is an index, which classifies weight-for-height in overweight and obesity in adults)(World Health Organization, 2003)
- The weight development throughout the relationship
- How does the couple split the work in the household (such as cooking, shopping for groceries etc.)?
- How was the T2DM diagnosed?
- How long has each spouse been taking part in the DMP?
- The development of the T2DM (change of medication, following diseases, complications etc.)
- Family anamnesis
- Level of education and current job situation.

### **2.2.3 Survey methodology**

Besides working out the topics of the questionnaire, one major task was to choose the methodology of the survey, before starting to convert the topic list into a questionnaire.

The following options were to be chosen from:

1. A personal face-to-face interview – either as paper-and-pencil (PAPI) or as computer assisted personal interview (CAPI)
2. A telephone interview – either as paper-and-pencil (PATI) or as computer assisted personal interview (CATI)

3. A mailed survey

4. (Online survey)

(Scholl, 2015, pp. 29–59)

#### The personal face-to-face interview:

The personal face-to-face interview is also called paper-and-pencil personal interviewing (PAPI). It is a form of a survey which is based on the presence of at least one interviewer, as well as at least one interviewee. (Scholl, 2015)

There are three different forms of personal interviews: personal in-home surveys, personal street intercepts and so-called classroom surveys. The latter two forms of this survey were not suitable for this kind of interview, because the interviewees were known and personal street intercept surveys are done with randomly chosen people in a public place. For a so-called classroom survey, the interviewees would have to be together in one room and would fill out a questionnaire themselves with an interviewer being present in order to help with difficulties. This is not applicable either, as it would be a much bigger effort with a lower success probability than just doing a personal in-home survey. (Scholl, 2015)

The personal in-home survey is the most frequently used personal interview, as it has fewer restrictions compared to the other two forms. (Scholl, 2015)

There are several advantages of a personal interview. The most important ones for this design are the following:

If the interviewee does not understand a question properly the interviewer has the possibility to explain what is meant.

Also, the interviewer can inquire further when a question is not answered sufficiently.

When facing complex instructions, the interviewer can guide the interviewee to an accurate response. (Scholl, 2015)

The disadvantages of a personal interview are:

The high costs and the high effort. (Scholl, 2015)

The interviewer himself or herself might also affect the interview negatively:

Because of the personal situation the interviewee might feel intimidated by the interviewer, which could have an effect on the answers.

The interviewer might misunderstand answers and write them down wrongly.

The interviewees might find it unpleasant letting an unfamiliar person into their home. (Scholl, 2015)

#### The telephone interview:

The interview by phone is a little bit less personal than the direct face-to-face interview, although a personal relationship is built between the interviewer and the interviewee. (Scholl, 2015)

The main condition, of course, is, that the interviewed couple can be reached by phone.

Advantages of the interview by phone are that:

It is much cheaper and it can be carried out with less effort than the face-to-face interview.

The data collection phase is shorter than a face-to-face interview.

The interviewees might find it more pleasant than having to let the interviewer in their house or apartment.

Similar to the face-to-face interview, the interviewer has the possibility to help the interviewee with comprehension problems.

The interview is more anonymous than the face-to-face interview which makes it more unlikely to get dishonest answers. (Scholl, 2015)

Disadvantages of the interview by phone are:

The questionnaire has to be designed in a relatively simple way (without visual scales or other visual aids).

It is more difficult to build up a personal relationship than in a face-to-face interview, which is necessary for sensible questions. (Scholl, 2015)

### The computer assisted interview

The computer assisted interview is a complement to the conventional forms of surveys. Its purpose is to make planning and execution cheaper and more efficient. (Scholl, 2015)

With computer assisted personal interviewing (CAPI) and computer assisted telephone interviewing (CATI), the interviewer uses a laptop reading the questions from the screen and types the answers straight into the laptop. (Scholl, 2015)

Advantages of computer assisted interviews are:

The data input and the data transmission are faster. The computer assistance helps the interviewer especially in complex questionnaires (helps preventing filtering errors).

The answers do not have to be inserted separately into the computer, which therefore prevents a major source of errors. (Scholl, 2015)

Disadvantages of computer assisted interviews:

Patients with little computer experience tend to refuse to participate at computer assisted interviews.

Due to the increased attention of the interviewer to the laptop, the interviewee may perceive the interview situation as disturbing.

The interview is less flexible, because the interviewer has to follow the logical guidelines from the computer. (Scholl, 2015)

### The mailed survey

For the written survey, there is no interviewer necessary, but the interviewees simply fill out the questionnaire, which was handed or sent to them. (Scholl, 2015)

This type of survey can be sent by post or via email, if all interviewees have working internet access. (Scholl, 2015)

Apart from the low cost and small effort of the written survey, it offers a few other advantages. However, one main disadvantage is the usually noticeable lower response rate than in other forms of surveys. (Scholl, 2015)

As a high response rate is crucial with a small group of patients, the written survey is not the most suitable for this work.

#### The online survey

The online survey is not suitable for this situation, because of the difficulty of creating one. Also, it has to be assumed, with this type of survey, that the target group has the technical know-how to participate. Due to the small number of patients this is not a given, so this survey was not appropriate. (Scholl, 2015)

The different methods of surveys and their advantages and disadvantages are summarised in the following table (Table 1):

**TABLE 1: METHODS OF SURVEYS IN COMPARISON**

<b>Method of survey⇒ Evaluation criteria↓</b>	<b>Personal</b>	<b>Telephone</b>	<b>Written</b>	<b>Online</b>
<b>Obligation of the situation</b>	High	Medium	Low	Low
<b>Control over the interview situation</b>	High	Medium	Low	Medium
<b>Anonymity</b>	Low	Medium	High	High
<b>Response rate</b>	High	Medium	Low	-
<b>Costs</b>	High	Medium	Low	Low
<b>Allowed length of questionnaire</b>	Medium	Low	High	High
<b>Allowed complexity of questionnaire</b>	Medium	Low	Medium	High
<b>Allowed complexity of questions</b>	High	Medium	Low	Low
<b>Allowed sensitivity of questions</b>	Low	Medium	High	High



The advantages and disadvantages of the different methods had to be put in relation to the given circumstances.

Due to the small number of patients one main criterion had to be the response rate. On the other hand, the small number of potential participants had the advantage of not causing a very significant cost, so that cost could play a subordinate role in finding the right survey method. The period of time in which the interviews had to take place was also flexible. Another major criterion was to get very accurate and correct answers in order to be able to evaluate the questionnaires properly.

These criteria led to the conclusion that the personal face-to-face interview and the telephone interview were the best options.

In order to achieve the highest possible response rate, it was decided to give the interviewees the option of choosing between those two interview forms.

The options were now to perform the interviews either with pen and paper or to do a computer assisted interview. For that decision and for the purpose of developing a perfectly suitable questionnaire in consideration of the thesis and the circumstances (such as the number of patients and the fact that the interviewees are all couples), Dr Jette Schröder, who works for GESIS (the Department of Survey Design and Methodology), was contacted. With her advice, and in consideration of the strength and weaknesses of the computer assisted interview, it was decided to do the pen and paper form of interview. Dr Schröder's opinion was that the main advantages of the computer assisted interviews appear especially in interviews with larger groups (faster data input and data transmission). Also, the advantage of visualisations would not be necessary in these interviews.

It was also decided to interview both spouses simultaneously.

Interviewing the couples together especially makes sense, when the couple is investigated as a unit. A joint interview provides a common reflective space, which contributes to the construction of rich data. (Bjørnholt and Farstad, 2014)

It also exhibits the so called tacit knowledge, meaning that if the couples have the opportunity to answer together, they are more likely to unveil forgotten knowledge. (Polak and Green, 2016)

Apart from these advantages, it has some practical benefits as it takes less time and makes it therefore more likely for the couples to take part. (Bjørnholt and Farstad, 2014)

This factor is a very important reason for the selection of this interview method, because due to the small number of patients, each interview is crucial.

#### **2.2.4 Developing the questionnaire**

Having now chosen the personal face-to-face interview and the telephone interview, the conversion of the list of topics to a questionnaire could be started. For this purpose, the close collaboration with Dr Schröder from GESIS was continued.

The questionnaire was planned to be a fully standardized survey in order to allow an accurate statistical comparison of the interviewees. Therefore, most items in the questionnaire would have to include a choice of answers.

Nevertheless, some questions should be formulated openly to give the interviewee the chance to give detailed information, where it seems to be necessary and constructive.

At the beginning of constructing the questionnaire, it had to be checked, if instruments of investigation about similar topics already existed.

These instruments might include already formulated questions, which could be adopted in this questionnaire. Although, if so, the questions had to be treated with care and would have to be screened for objectivity, reliability and validity. (Raab-Steiner and Benesch, 2015, p. 47)

Especially the panel analysis of intimate relations and family dynamics (PAIRFAM-study) was observed thoroughly for suitable questions. This study offers different questionnaires (codebooks) dealing with different topics. One of the key aspects of the PAIRFAM-study is partnership, on which a questionnaire was developed, including questions regarding the general life in a partnership. (Brüderl *et al.*, 2014)

This codebook provided the basis of the developed questionnaire, although only one item was adopted word-for-word (division of labour).

Also, a questionnaire regarding food intake was reviewed and ideas were taken from it, none of the items were adopted word by word. (German Institute of Human Nutrition Potsdam Rehbrücke, 2017)

The questions regarding other topics, such as medical issues, medicine intake and diabetes complications, were developed by myself in close collaboration with Dr Jette Schröder from GESIS and Dr Andrea Werdecker and my doctoral thesis supervisor Prof Dr Ulrich Mueller from the then Institute for Medical Sociology and Social Medicine at Philipps University, Marburg.

### **2.2.5 Pretest**

A pretest should be carried out in order to check the following issues:

- Comprehensibleness of the questions.
- Do the answer possibilities suit their questions well?
- Is the length and duration suitable?
- Are the questions constructive towards the hypotheses?
- Are the items in a correct order?
- Is the layout clearly arranged?
- Are the instructions for the interviewer clear?

(Porst, 2014, p. 189; Raab-Steiner and Benesch, 2015)

A standard observation pretest could not be done in this case as the questionnaire design could not be tested on randomly chosen spouses with T2DM. In order to test the questionnaire on these issues anyway, it was tested on 20 fellow students. That way it was possible to improve some items and establish a routine as an interviewer.

### **2.2.6 Interviews**

All 17 couples identified by the same address in the data set were contacted.

Of the 7 couples, who agreed to be interviewed again, 4 (3 couples plus the surviving widow of the fourth one – see above) also agreed to be visited personally by me. The remaining 3 couples preferred a telephone interview,

which was held by Dr Andrea Werdecker, who, at that time, was a Research Associate at the Institute of Medical Sociology and Social Medicine at the Philipps University of Marburg.

All interviews, telephone and personal, went as planned. They were held with both partners (with the exception of the couple where the husband had deceased) simultaneously and each interview took about 20 minutes, but never more than 30 minutes.

Based on the interview results the different hypotheses were formulated on how the mechanism can be assumed, in which a spouse can be a risk factor for developing a T2DM.

## **2.3 Data analysis approaches**

The set of data of the CDRM study can be divided into two groups, of which one can be subdivided again:

- Couples within the set of data (18 couples – 36 individuals)
  - Couples, who have been interviewed (7 couples – 14 individuals)
  - Couples, who have not been interviewed again (11 couples - 22 individuals)
- Individuals, with unknown partner status (362 individuals).

In order to investigate a causal association between a spouse being a risk factor, the groups have to be observed and compared to each other. That means, that the following results will be described:

- Comparison of interviewed spouses with not-interviewed spouses
- Examination of couples
- Comparison of all spouses with the other individuals in the set of data
- Case series study of the 7 in-depth-interviewed spouses.

### Comparison of interviewed spouses with not-interviewed spouses:

The objective of comparing the interviewed spouses with the not-interviewed ones is to determine whether there might be a medical reason on why patients declined the interview. An example for a medical reason would be if there was a difference in age or year of diagnosis, which could indicate a larger progress of the disease.

If, however, the spouses do not differ in

- year of diagnosis
- year of birth
- possible time of 'infection'
- the comparison of HbA1c,

then it can be assumed, that there is no medical reason, why some of the spouses could not be interviewed. In that case, a generalization of the information obtained from the interviewed couples to all couples in the set of data could be very carefully made.

If the comparison of the interviewed and not-interviewed couples would however suggest a medical reason for a declined interview, that would have to be taken into account in the analysis. The data set of the not-interviewed spouses would then have to be handled with even greater care. A carefully made generalization from the collected data would not be possible.

### Examination of couples:

When it comes to examining the identified couples (both interviewed and not interviewed) there is especially one interesting criterion to look at. This is the temporality, which is a crucial criterion to see a possible causal association. Therefore, the first step was to compare the year of diagnosis between the spouses. There has to be a gap of at least some years, to be able to talk about a contagion of lifestyle and health behavioural habits.

An additional main aspect concerning the temporality the progress of the disease, as T2DM is a progressive disease. That means that it is likely that the longer one has the disease, the more progressed it is. This can be observed by

looking at the value of HbA1c, sequelae (i.e. microangiopathies) and the medical treatment.

If this value can be established, the next step is to see if these differences can be attributed to the sex of the patients. This could then be a sign that not a spouse in general but a spouse of a particular sex may be the risk factor for the development of a Type 2 Diabetes mellitus.

#### Comparison of all spouses with the other individuals in the set of data:

From the 398 subjects of the CDRM study a subsample was drawn in order to compare the 36 individuals in the 18 married couples with them. For each 18 males and 18 females in the patient-marriages, three other males and three other females, all with the same birth year, accordingly were randomly sampled, ending up with a study population of 144 subjects: three controls for each subject.

For all 18 males (1 born 1940, 4 in 1941, 2 in 1942, 1 in 1943, 1 in 1944, 1 in 1945, 1 in 1946, 1 in 1950, 1 in 1951, 1 in 1952, 1 in 1953, 1 in 1954, 1 in 1955, 1 in 1958) controls with exactly the same year of birth could be sampled.

For the 16 females (2 born in 1942, 1 in 1943, 1 in 1945, 1 in 1946, 1 in 1947, 1 in 1948, 2 in 1949, 1 in 1951, 1 in 1952, 1 in 1953, 2 in 1954, 1 in 1955, 1 in 1964) controls with exactly the same year of birth, for one female born in 1963, three controls born in 1962, 1963, 1964, for another female born in 1965, three controls born 1964, 1964, 1966 could be sampled.

Next, alongside each real married couple, three fictitious control couples were generated. These four couples (one real, three controls) shared the same birth year for the male and for the female partner (with the two exceptions mentioned above). Therefore, the final data set consisted of 18 real and pairwise-matched 54 control couples.

All data analyses were performed with this pairwise-matched sample, guaranteeing an optimal control of birth year, age (since in the main study first-patient-in date was in January 2009 and last-patient-in date in May 2011) and age difference between spouses.

Using this design, even with a much larger number of cases, generalizable findings on prevalence and incidence of T2DM in married couples would only be possible with limitations. However, since nothing is currently known about frequencies and age distribution of T2DM in married couples, these limitations have to be accepted.

The results of comparing the subjects in the patient-marriages with the controls can be found in the results.

These comparisons will include the age of patients when diagnosed with Type 2 Diabetes mellitus and the progress of the disease (using HbA1c values).

#### Case series study of the 7 in-depth-interviewed spouses:

Based on the results of these approaches, the interviewed couples have to be looked at closer.

If the results show that a causal association is likely, the knowledge about the spouses' lifestyle could give information on how the causation might work within the relationship and whether the information could give an idea on how the contagious lifestyle can be defined.

If the results show that a causal association is not likely, the data of the interviewed couples should be examined nevertheless. This is to see whether, there is any evidence of the hypothesis, that both partners in the group of spouses already lived with risk factors of T2DM from the beginning of their relationship. The body mass index (BMI) of the couples and their weight development over the years is of interest here.

The evaluation is made using different tests in the program of SPSS statistics 23:

#### **Chi-Squared-Test:**

The Chi-Squared-Test is a statistical test method for screening the independency of variables in a cross-classified table.

This test serves to analyse frequencies, which makes that test multifunctional as frequencies can be determined in any scale of measurement.

The null hypothesis states that the results are independent from each other, whereas the alternative hypothesis states that there is a dependency.

The general idea is to compare the observed frequencies with the expected values from the null hypothesis.

The calculated  $\chi^2$  -value tends to 0 when the null hypothesis is true and gets larger the more the observed values differ from the expected values.

(Weiß, 2013, pp. 200–205; Bühl, 2016, pp. 305–307)

### **Mann-Whitney-U-Test:**

This test is an alternative to the t-test used for a comparison of two independent samples. It is a non-parametric test, which is used for looking at differences between such samples. (Field, 2013, p. 878; Bühl, 2016)

A big advantage of this non-parametric test is that the statistical population does not have to be normally distributed.

The null hypothesis states that there is no difference between the compared values of the two independent samples.

All values from both samples are ranked in ascending order and provided with numeric ranks. The ranks are added up for each sample (A and B) separately ( $R_A$  and  $R_B$ ) in order to calculate the statistic U for each sample with the following formula:

$$U_A = R_A - \frac{n_A(n_A + 1)}{2}$$

$$U_B = R_B - \frac{n_B(n_B + 1)}{2}$$

The smaller value is the test statistic, which is used to either confirm or refute the null hypothesis. (Harms, 2012, pp. 339–340)

### **Alpha-error correction:**

An Alpha-error or Type I error occurs when the null hypothesis is refuted, although it is true.



The probability of rejecting the null hypothesis although its true is the significance level  $\alpha$ . This probability increases when multiple testing is done within one sample as it will be done in this study. The Alpha-error correction is a method to counter this problem.

A simple way to do so is using the Bonferroni correction, which states that the results are only statistically significant, if the following is true:

$$p < \frac{\alpha}{k}$$

p: The p-value quantifies the probability that a test result is equal to or greater than the actual observed results, when the null hypothesis is true.

k: number of tests done.

The disadvantage of this procedure is the increase of the probability of a type II error. A type II error ( $\beta$ -error) occurs if the null hypothesis is accepted, although the alternative hypothesis is true.

(Harms, 2012, pp. 322–323; Weiß, 2013, pp. 165–174)

The dataset of 36 married couples with the 108 pairwise matched control couples was prepared by the supervisor Prof. Mueller. Analysis of these data was carried out in several joint multi-hour sessions in front of the monitor with the supervisor in Wiesbaden. Results were independently checked and critically discussed by me, all remaining errors are mine.

## 3 Results

### 3.1 Comparing interviewed spouses with not-interviewed spouses

The comparison of the interviewed couples with the not-interviewed couples did not show any differences (cf. Tables 2 & 3). There were:

- no difference in year of diagnosis (neither for females nor for males)
- no difference in year of birth
- no difference in possible contagious-time (time difference between first diagnosis of male and female partner)
- no difference in individual HbA1c levels nor in intra-couple differences in HbA1c levels

But there was a difference in the age difference when diagnosed with T2DM between male and female: In the interviewed couples the age difference between the spouses was much smaller than in the not-interviewed couples as seen in Table 3. This, however, has no impact on the interpretation of the results for the following reason:

- Due to the small number of cases one runaway value has a big impact on the mean – which is the case here:  
There is one considerable older male with a younger female partner in the non-interviewed couples. This increases the mean in age difference when diagnosed with Type 2 Diabetes mellitus

As the couples do not differ in any other comparison point, this variance can be ignored.

**TABLE 2: COMPARISON BETWEEN INTERVIEWED AND NOT-INTERVIEWED COUPLES**

<b>Interview Status</b>		<b>Male: Year when diag.</b>	<b>Male: HbA1c</b>	<b>Female: Year when diag.</b>	<b>Female: HbA1c</b>
<b>No</b>	<b>Mean</b>	2003.91	6.280	2001.1	6.836
	<b>N</b>	11	10	10	11
	<b>Std. Deviation</b>	4.25334	0.5116	8.089	0.8381
<b>Yes</b>	<b>Mean</b>	2003.42	6.285	2001.9	6.716
	<b>N</b>	7	7	7	6
	<b>Std. Deviation</b>	5.47288	0.67683	6.6188	1.037
<b>Total</b>	<b>Mean</b>	2003.72	6.282	2001.4	6.794
	<b>N</b>	18	17	17	17
	<b>Std. Deviation</b>	4.61208	0.5648	7.3063	0.8799

Table Explanation (Table 2-8 and Table 11):

Mean: Sum of all values divided by the number of values

N: Number of Patients

Standard Deviation: Measurement of divergence of a set of values.

Couple status: Yes: Patients, who have been identified as couples in the set of data  
No: Patients, who have been randomly assigned to the couples

Interview status: Yes: Couples from the data set, which have been interviewed  
No: Couples from the data set, which have not been interviewed

(Harms, 2012; Weiß, 2013)

**TABLE 3: COMPARISON BETWEEN INTERVIEWED AND NOT-INTERVIEWED COUPLES**

<b>Interview Status</b>		<b>Diff. in age: Male-female when diag.</b>	<b>Male: Age when diag.</b>	<b>Female: Age when diag.</b>
<b>No</b>	<b>Mean</b>	8.8000	58.363	48.700
	<b>N</b>	10	11	10
	<b>Std. Deviation</b>	6.9889	5.4639	9.4757
<b>Yes</b>	<b>Mean</b>	1.1429	55.142	54.000
	<b>N</b>	7	7	7
	<b>Std. Deviation</b>	8.8774	2.4784	7.1879
<b>Total</b>	<b>Men</b>	5.6471	57.111	50.882
	<b>N</b>	17	18	17
	<b>Std. Deviation</b>	8.4922	4.7265	8.7812

This leads to the assumption that there are no medical differences in the spouses who were interviewed and those who were not interviewed.

Because of these similar tendencies, it was now possible, to very cautiously generalize the findings obtained from the 7 interviewed couples to all 18 couples in the set of data.

### **3.2 Examining couples**

In both interviewed and not-interviewed couples an inverse correlation between the year of diagnosis and the value of the glycated haemoglobin (HbA1c) was observed. This finding suggested that the earlier the diagnosis the more advanced the diabetes. It also indicated that the value of HbA1c is a valid

measurement for the progress of the disease. This inverse correlation could also be assumed with the patients not known to be married to a T2DM patient.

In order to talk about a contagious lifestyle there would have to be a large difference in the year of diagnosis between the sexes. The results, however, show that there is no sign of sex relation in the year of diagnosis. It is even the other way around as most of the couples in the set of data received the diagnosis of T2DM within two years of each other.

This temporality (the fourth of the Bradford Hill criteria) is a condition for a causal association and cannot be observed in this case.

Also, the males and females within the couples did not show differences in the severity of the disease nor in how far the disease had proceeded, meaning that neither the value of HbA1c nor the medication showed significant differences between the males and females.

It can be said that the value of HbA1c is suitable as a factor for comparative value as it can be assumed that all of the patients in the set of data were receiving the same medical care. This is because all of them were taking part in a disease management programme and the couples even shared the same doctor.

This means that it is very likely that there is no contagion in lifestyle happening within the couples.

### **3.3 Comparing couples with internal controls from the CDRM data set**

The couples were randomly assigned to each 3 females and 3 males from the CDRM data set, who were born in the same year. This was done in order to reveal possible differences, which might be pointing out causality.

The group of couples only differed in two points from the internal controls from the CDRM data set.

- There was no significant difference in the age of the patients
- There was no significant difference in the age of diagnosis of females

- There was no significant difference in the value of HbA1c of females.

There was, however, a difference in the age of diagnosis and the HbA1c of males.

The males from the internal control were on average 4 years younger when diagnosed and had a lower HbA1c than the males from the couples.

These comparisons can be observed in the following two tables (Table 4 & 5).

If, however, male patients with very high HbA1c values of 7.5% and more were removed from the analysis (13 from the control group and only 1 from the couples), then there was no difference between couples and the randomly assigned patients with identical year of birth anymore in (cf. Tables 6 & 7):

- Year and age of diagnoses
- HbA1c for male and female
- Difference between years of diagnoses of spouses.

**TABLE 4: COMPARISON BETWEEN COUPLES AND RANDOMLY ASSIGNED PATIENTS FROM THE STUDY**

<b>Couple Status</b>		<b>Male: Year when diag.</b>	<b>Male: HbA1c</b>	<b>Female: Year when diag.</b>	<b>Female: HbA1c</b>
<b>No</b>	<b>Mean</b>	1999.58	6.867	2000.2	6.850
	<b>N</b>	53	53	49	53
	<b>Std. Deviation</b>	8.07997	0.9681	6.9432	0.8818
<b>Yes</b>	<b>Mean</b>	2003.72	6.282	2001.4	6.794
	<b>N</b>	18	17	17	17
	<b>Std. Deviation</b>	4.61208	0.5648	7.3063	0.8799
<b>Total</b>	<b>Men</b>	2000.63	6.725	2000.5	6.837
	<b>N</b>	71	70	66	70
	<b>Std. Deviation</b>	7.5465	0.9188	7.0016	0.8752

**TABLE 5: COMPARISON BETWEEN COUPLES AND RANDOMLY ASSIGNED PATIENTS  
FROM THE STUDY**

<b>Couple Status</b>		<b>Diff. in age: Male-female when diag.</b>	<b>Male: Age when diag.</b>	<b>Female: Age when diag.</b>
<b>No</b>	<b>Mean</b>	3.6042	53.018	49.776
	<b>N</b>	48	53	49
	<b>Std. Deviation</b>	11.175	8.4387	8.9029
<b>Yes</b>	<b>Mean</b>	5.6471	57.111	50.882
	<b>N</b>	17	18	17
	<b>Std. Deviation</b>	8.4922	4.7265	8.7813
<b>Total</b>	<b>Mean</b>	4.1385	54.056	50.061
	<b>N</b>	65	71	66
	<b>Std. Deviation</b>	10.515	7.8447	8.8176

Among men with a high value of HbA1c, there might be some single men without the support married men may receive from their spouses. Those men may be in a particularly poor health condition and, therefore, the disease was diagnosed earlier and the progression was more advanced when these men entered the study.

**TABLE 6: COMPARISON BETWEEN COUPLES AND RANDOMLY ASSIGNED PATIENTS  
FROM THE STUDY (AFTER REMOVING PATIENTS WITH AN HbA1c >7,5)**

<b>Couple Status</b>		<b>Male: Year when diag.</b>	<b>Male: HbA1c</b>	<b>Female: Year when diag.</b>	<b>Female: HbA1c</b>
<b>No</b>	<b>Mean</b>	2001.6	6.526	2000.1	6.89
	<b>N</b>	41	42	40	41
	<b>Std. Deviation</b>	6.4566	0.5831	7.1584	0.908
<b>Yes</b>	<b>Mean</b>	2003.7	6.200	2001.5	6.83
	<b>N</b>	16	16	16	15
	<b>Std. Deviation</b>	4.4795	0.4661	7.5185	0.920
<b>Total</b>	<b>Men</b>	2002.2	6.436	2000.5	6.88
	<b>N</b>	57	58	56	56
	<b>Std. Deviation</b>	6,006	0.5687	7.2236	0.904



**TABLE 7: COMPARISON BETWEEN COUPLES AND RANDOMLY ASSIGNED PATIENTS FROM THE STUDY (AFTER REMOVING PATIENTS WITH AN HbA1c >7,5)**

<b>Couple Status</b>		<b>Diff. in age: Male-female when diag.</b>	<b>Male: Age when diag.</b>	<b>Female: Age when diag.</b>
<b>No</b>	<b>Mean</b>	4.615	54.69	49.75
	<b>N</b>	39	41	40
	<b>Std. Deviation</b>	10.94	7.827	9.029
<b>Yes</b>	<b>Mean</b>	5.687	56.50	50.81
	<b>N</b>	16	16	16
	<b>Std. Deviation</b>	8.769	4.289	9.064
<b>Total</b>	<b>Men</b>	4.927	55.19	50.05
	<b>N</b>	55	57	56
	<b>Std. Deviation</b>	10.29	7.027	8.969

This means that it is unlikely that there is a difference in the development of T2DM between patients with ill spouses and the rest of the patients. Again, this finding suggests that there is no causal association.

Taking the Bradford Hill criteria into account, the one condition that has to be fulfilled in order to see causality is 'temporality'. Another condition is 'biological gradient' (Dose-Response-effect).

Therefore, if a T2DM patient 'infects' his or her spouse, then the dose would be the duration of the partnership, because as mentioned earlier the exposure time to risk factors increases the risk of developing T2DM. In this case an "infection" cannot go on very fast. Therefore, the risk for an initially healthy partner to develop T2DM increases the longer the marriage (exposure) goes on.

The assumption would be, that in couples, the difference in years at age of diagnosis, as well as the difference in calendar years of diagnosis would be higher in couples than in the randomly assigned patients of the control group.

However, the opposite has been observed in the analysis. On average, in randomly assigned couples, males and females were more age years as well as calendar years apart than in real couples. The difference in calendar years was even significantly smaller in real couples as can be seen in Table 8.

**TABLE 8: COMPARISON BETWEEN COUPLES AND RANDOMLY ASSIGNED PATIENTS IN AGE DIFFERENCE OF DIAGNOSIS AND IN YEARS BETWEEN DIAGNOSIS**

<b>Couple Status</b>		<b>Difference in age when diagnosed</b>	<b>Years between male and female diagnosis</b>
<b>No</b>	<b>Mean</b>	9.2708	7.5208
	<b>N</b>	48	48
	<b>Std. Deviation</b>	7.09732	6.75400
<b>Yes</b>	<b>Mean</b>	8,1176	4,2353
	<b>N</b>	17	17
	<b>Std. Deviation</b>	5.99877	4.58979
<b>Total</b>	<b>Men</b>	8.9692	6.6615
	<b>N</b>	65	65
	<b>Std. Deviation</b>	6.80066	6.39403

In conclusion, it can be said that the shorter time gaps in ages at diagnoses as well as in calendar years in diagnoses in couples may be interpreted as evidence that these spouses were taking care of one another and encouraging each other to see a doctor once the first partner received the diagnosis.

All these observations support the interpretation that there is assortative mating, rather than causal association in married couples where both are suffering from T2DM.

### **3.4 Case series study of the 7 in-depth-interviewed couples**

The results presented so far suggest that there is no causal association between a spouse being a risk factor for their partner to develop a T2DM themselves. Thus, the 7 patients will now be observed for any support for the alternative 'assortment' hypothesis.

In order to do so, the main risk factor of diabetes, which is obesity, will be looked at in the 7 couples.

Of the 7 females in the couples, only two had healthy weights (BMI: <25.0). The 5 remaining females were obese, with a BMI of at least 32.8 and 3 of them with a BMI >39.0 (cf. Table 9).

All of the 7 males were overweight or obese, with a BMI range from 26.0-44.8. Two of the men were overweight (BMI 25.1-30.0) and 5 were obese (BMI >30.0) (cf. Table 10).

None of the couples, males or females, stated that they lost weight over the time period of marriage and none stated that their weight increased erratically. All of them gave either of the two answers: 'weight did not change' or 'weight increased constantly' (cf. Tables 9 & 10).

The weight of two females and three males grew constantly over the time period of marriage. Apart from one female, who did not answer the question, the remaining spouses said that their weight stayed the same over the years of their marriage (cf. Tables 9 & 10).

Comparing the weight development of spouses, the following can be seen:

Of the husbands of the two females with increased weight over the years of marriage, one also stated that he had gained weight. The other one maintained his weight.

Of the 14 individuals 8 maintained their weight and 5 gained weight over the years of marriage. Only two individuals were not overweight or obese.

This data suggests, that it is very likely that most individuals in this set of data were overweight or obese, before entering the relationship or marriage.

**TABLE 9: FEMALES FROM THE INTERVIEWED COUPLES**

<b>Weight (kg)</b>	<b>Height (cm)</b>	<b>BMI</b>	<b>Weight change</b>
114	169	39.9	Increased constantly
102	160	39.8	No change
84	160	32.8	No change
63	165	23.1	No change
55	153	23.5	-
105	160	41.0	No change
105	173	35.1	Increased constantly

**TABLE 10: MALES FROM THE INTERVIEWED COUPLES**

<b>Weight (kg)</b>	<b>Height (cm)</b>	<b>BMI</b>	<b>Weight change</b>
75	170	26.0	No change
90	172	30.4	No change
98	175	32.0	No change
112	175	36.6	Increased constantly
142	178	44.8	Increased constantly
102	165	37.5	Increased constantly
85	171	29.1	No change

**Daily activities: Food preparation / nutrition / shopping / housekeeping**

In the majority of cases (5) a conventional division of responsibilities was observed, with the wife being the family and home manager and the husband

lending a helping hand. In a minority of cases (2) there was more or less equal sharing of responsibilities. This proportion reflects the present social reality in Germany.(Pötzsch and Sommer, 2016, pp. 426–433)

### **Work situation**

Only one man was still in an active job. All of the other 13 interviewees were retired. Three of those were receiving disability pensions.

### **Diabetes in the Family**

Three females and four males did not report Type 2 Diabetes mellitus cases in the family. Two females reported two, two reported three cases in the family. Two males reported two, one reported four cases in the family.

### **Duration and Satisfaction with DMP enrolment:**

Five couple enrolled in the same year – possibly at the same date. In one couple, the husband enrolled one year earlier, in one the husband enrolled three years later. On average, the couples had entered the programme five years before the interview in 2014.

All couples reported the same degree of satisfaction with the care within the programme: five reported high, two very high satisfaction.

### **Diagnosis**

In six females and in six males the diagnosis of T2DM was made in the course of a general screening examination ('incidentally at a routine check-up'). One male and one female saw a physician because clinical symptoms were present. The female reported that, being informed about her husband's symptoms, she was able to perceive and recognize specific symptoms in herself.

## **Complications**

One male reported a diabetes specific eye problem, sensibility disorders, a kidney transplant and a leg amputation during the last six months; no other male reported any complication. One female received a coronary heart disease diagnosis; no other female reported any complication.

## **Medication**

One male was not on medication, only on dietary management. Two males were on oral medication alone, one male was on insulin alone, two males were on insulin plus oral medication.

Two females were not on medication, only on dietary management. Two females were on oral medication alone; three females were on insulin plus oral medication.

The following table (Table 11) shows the medication taken by the patients. There were no raw differences between couples and non-couples.

## **Nutrition and food patterns**

Due to a large number of possible answers and a small number of cases the questions about nutrition and food patterns could not be evaluated reasonably.

**TABLE 11: COMPARISON OF CURRENT MEDICATION BETWEEN COUPLES AND RANDOMLY ASSIGNED PATIENTS FROM THE STUDY**

<b>Couple Status</b>		<b>Insulin or Insulin Analogs</b>	<b>Glibenclamid</b>	<b>Metformin</b>	<b>Other Oral Antidiabetic Medication</b>
<b>No</b>	<b>Mean</b>	0.21	0.11	0.62	0.11
	<b>N</b>	53	53	53	53
	<b>Std. Deviation</b>	0.409	0.320	0.489	0.320
<b>Yes</b>	<b>Mean</b>	0.29	0.12	0.59	0.18
	<b>N</b>	17	17	17	17
	<b>Std. Deviation</b>	0.470	0.332	0.507	0.393
<b>Total</b>	<b>Mean</b>	0.23	0.11	0.61	0.13
	<b>N</b>	70	70	70	70
	<b>Std. Deviation</b>	0.423	0.320	0.490	0.337

In a long battery of metabolic, acute clinical or anamnestic parameters, there were no raw differences between males in the couples and their controls. The few such raw differences between females in the couples and their controls may indicate that the females in the couples were slightly heavier and sicker than their controls, but none of the reported significance results would survive an alpha-error correction, mandatory in this case of multiple testing.

Thus, we can conclude that the health as well as the prescription status of the married couples was the same as for their controls.

## 4 Discussion

### 4.1 Differences and conformity between these results and the results found and reported in the research literature

Firstly, the results were put into a scientific context with observations and results from other studies. This was carried out with the following two approaches.

On the one hand, the results were compared to the studies, which found a high prevalence of T2DM in spouses. These studies, however, do not include hypotheses on why this was the case.

That is why, on the other hand, it was necessary to compare the results of this research with the studies dealing with an increased risk of other diseases in spouses. The focus was placed on the differences and conformities of why the elevated risk was assumed.

The main conformity between this study and the previous studies, which show a high prevalence of T2DM in spouses, was exactly that high prevalence. In the studies reviewed, there was an increased relative risk for a spouse to develop T2DM from 1.3 up to 3.4. (Di Castelnuovo *et al.*, 2009; Hemminki *et al.*, 2010; Leong, Rahme and Dasgupta, 2014; de Visser *et al.*, 2015)

In this study the incidental finding of an elevated number of spouses could not be quantified (see section 1.1), however, since at least 36 individuals of 398 in the data set were married, this finding strengthens the observations from the other studies.

These studies, however, did not broach an explanation for their observations. Hemminki *et al.* (2010) vaguely referred to 'environmental factors' as a reason for the increased prevalence in spouses, but none of the studies went into depth.

These findings of an elevated risk for spouses has only limited clinical relevance, if the cause has not been observed.



Therefore, these mentioned studies build the foundation for this work. This dissertation is an addition to the previously established findings in order to increase the clinical relevance.

As there are no other studies making similar observations, except with reference to different diseases, it made sense to compare the results to these other studies. This was because many risk factors can be found in lifestyle and health behaviour (i.e., weight and eating habits in cardiovascular diseases). (International Diabetes Federation, 2017, pp. 22–24)

Some of these other studies assume assortative mating as a reason for the increased prevalence of a disease, which conforms with the findings in this research. (Grant *et al.*, 2007)

Other studies have suggested a contagion in lifestyle habits and health behaviour in spouses, which then leads to an adaption of risk factors between the partners. (Homish and Leonard, 2005; Jurj *et al.*, 2006)

A very interesting study has been made by S.E. Wilson (2002), 'The health capital of families: an investigation of the inter-spousal correlation in health status', in which the health status in spouses in later life have been documented and analysed. (Wilson, 2002, pp. 1157–1172)

Wilson's general finding was that an inter-spousal correlation in health status was demonstrated. He suggested that diseases do not spread randomly over the population, but appear rather in marriages to other sick people. (Wilson, 2002)

Wilson's conclusion takes many different factors in account. Apart from the known phenomenon of assortative mating, he proposes the possibility of developing health behaviours and lifestyle habits together.

Wilson's assumption differs from the one made in this research, which puts the focus on a mutual lifestyle change, rather than on a contagion in lifestyle.

In my opinion, Wilson's findings would be a very valid approach to this research work. However, the collected data and the low number of couples in this research does not allow such an extension of this work to be made.

## **4.2 New insights**

Other studies have shown a higher prevalence of T2DM in spouses without observing the reasons for that.

Differing from those previous studies, a putative causation is refuted in this dissertation.

The reason can rather be explained by assortative mating. Meaning that people with similar circumstances of life (such as socio-economic status, obesity and low physical activity) are likely to mate among themselves. This leads to a higher probability of developing T2DM for both partners.

This can be a very valuable finding, as it can be a step forward in the prevention of a widespread and growing disease. With this knowledge, it can be recommended that attention should also be turned on the spouse, as soon as a married person gets diagnosed with T2DM.

On the other hand, this study shows that the elevated risk of developing a T2DM, when the partner already suffers from one, is very unlikely to be due to a causal association. This means, there are no signs of a contagion of lifestyle habits between the partners.

## **4.3 Limitations of this case series**

These results have to be interpreted with great care for the reasons outlined below.

The number of cases in the set of data was rather small and as mentioned before (see section 1.2.2), case series should not be generalized without careful consideration.

The individuals were all drawn from a set of data of four different physicians in and around Mannheim, Germany, so that the information obtained only represents a small area.

Nevertheless, the results were very clear, and even with the small number of cases, it can be assumed that they are reproducible in other study populations

as well. Therefore, a general indication of why there is an elevated risk for spouses can be given.

However, the data set does not give enough information about the couples and their lives together in order to investigate more detailed tendencies of lifestyle changes. So, a possible mutual change in lifestyle, leading to an increased risk for T2DM, cannot be studied in this group of spouses.

## **5 Conclusion**

### **5.1 What has been previously been established?**

In the previous literature, it has been established that a marriage partner with T2DM is a statistical risk for developing T2DM oneself. Such a risk, however, cannot be observed in the dataset analysed here, since this dataset contains only subjects with T2DM.

### **5.2 What does the study add?**

What in principle could have been observed in the dataset analysed here, but actually was not observed, is support for the guiding hypothesis in the research question, namely that – by a hypothetical contagiousness of lifestyle habits – there might be a causal relation between a T2DM patient as a spouse and the developing of T2DM oneself.

Rather, the findings in this study suggest, that there may be assortative mating by lifestyle habits, but no contagiousness of lifestyle habits within marriages, after partners have already found each other.

Together with the increased risk for own T2DM once married with a manifest T2DM patient, which has been replicated in various studies, it can be stated that a manifest T2DM marriage partner may be a marker, but not a causal agent for an increased risk of T2DM.

### **5.3 Limitations of the study**

The number of cases is sufficient for demonstrating only a few effects with statistical tests. However, the observed patterns permit the perception of a few robust trends.

Many possibilities for bias may, after all, not have materialized. Of all 18 married couples with T2DM observed within n=398 outpatients in a Managed Care Outpatient, all went to the same medical practice, although altogether 17 medical practices – some with up to five physicians – from the same region

participated in the study. There was no case of a couple in the study population presenting to different participating medical practises. Thus, the number of marriage couples with both having T2DM, but (1) with one partner presenting to a medical practice not in the study, AND (2) other assortment or causality findings than observed here, may be limited, after all.

The results show that the criterion 'sine qua non', which is temporality, was not verifiable in the couples. The difference in 'year of diagnosis' between males and females was not large enough to assume a causal association.

This, however, only applies to the causal association, referring to the Bradford Hill criteria or, in other words: There is no causation between factor (spouse with T2DM) and effect (elevated risk for own T2DM).

## **5.4 Practical consequences of the study**

Although living with a T2DM patient is not a risk per se for developing the disease, from the viewpoint of primary as well as secondary prevention, it is advisable to target spouses of T2DM patients as a high-risk group, because people with an increased risk for the disease may have selected themselves into such marriages by assortative mating. Therefore, any married T2DM patient should be used as a transmitter of relevant information to their spouse, and the spouse should be invited for a screening test.

Yet, this does not mean that a spouse with T2DM does not elevate the risk of an own development of the disease. The opposite is true: If a partner suffers from T2DM, one faces an increased risk of developing T2DM as well.

The reason is that it is very probable that people with already very similar lifestyles, especially eating habits and lack of physical activity, are more likely to establish a relationship.

This phenomenon is called assortative mating and has already been described in other studies (see section 1.2).

Therefore, it is likely that the following hypothesis is valid:

T2DM patients lead to an increased risk for their partner developing T2DM, because the partner is likely to share similar risk factors.

The research question,

‘Do the partners in T2DM couples resemble each other more closely in the clinical and lab parameters of the disease than in randomly taken pairs of opposite sex subjects from the same study population of T2DM patients enrolled in the specific T2DM DMP?’

can also be answered in the negative. There are neither differences in the clinical nor in the lab parameters of the couples and the randomly chosen T2DM patients from the data set.

This dissertation with these results could be a solid foundation for another study to build upon. The approach could be to investigate newlywed couples on similarities in weight, health behaviour and physical activities. This could possibly verify what is strongly indicated with the results presented here. These couples could then, years later, be checked upon in a follow-up study in order to see the development of risk factors or if T2DM has been developed by one or both partners.

Also in this study, the lifestyle change could be observed over the years: whether the lifestyle did not change at all or whether the lifestyle of both couples might have changed simultaneously over the years.

In conclusion, it can be said that the Type 2 Diabetes mellitus patient is not a causal risk factor in the narrower sense, but rather a marker of an own T2DM conducive lifestyle.

Therefore, it obviously is a recommendation to invite the partner of a T2DM patient to a screening early on and regularly.

Apart from this screening it seems crucial that the partner of a T2DM patient should also be able to take part in nutritional counselling and may even take part in the partners disease management programme.

## 6 Summary

As has been established in previous research that living in a relationship with a person suffering from Type 2 Diabetes mellitus increases the risk of developing the disease yourself. However, the reason for this increased risk has not been observed in any of these studies.

A large study (n=398), which had the objective to compare the impact of a new care programme in the context of a disease management programme of T2DM patients, also showed a large number of diabetic couples. This study population was used in this study to research the potential causation of the increased T2DM risk in couples. The hypothesis was therefore: 'A person with T2DM is causal for the elevated risk of his or her spouse to develop T2DM as well'.

In order to distinguish, in observational studies, whether there are causal or non-causal associations in the genesis of a disease the Bradford Hill criteria were utilized and the research attempted to apply each criterion to this set of data to see whether a causality was likely.

Firstly, all couples from the set of data were identified by matching their last names and addresses (18 couples, 36 individuals). These couples were then contacted and invited to join an interview in order to gain as much information about their mutual lives and T2DM risk factors as possible. Not all couples agreed to participate in an interview, creating 3 data set groups:

- Interviewed couples.
- Not-interviewed couples.
- The patients from the large set of data not known to be in a relationship with a T2DM patient.

These 3 groups were then observed and compared in order to see differences and similarities between and within them. These observations were analysed taking into account the Bradford Hill criteria.

The results show that the hypothesis does not seem to be true. There does not seem to be a causal association between a partner developing T2DM when married to a T2DM patient. The reason can rather be explained by assortative

mating, meaning that people with similar circumstances of life (such as socioeconomic status, obesity and low physical activity) are likely to mate among themselves.

In conclusion, it can be stated that a marriage partner with a manifest T2DM may be a marker, but not a causal agent for an increased T2DM risk.



## 7 Zusammenfassung

In verschiedenen bereits durchgeführten Studien zeigte sich ein erhöhtes Risiko an einem Diabetes mellitus Typ 2 zu leiden, wenn der Partner von dieser Erkrankung bereits betroffen ist. In keiner dieser Studien wurde jedoch die Ursache dafür gesucht oder gefunden.

Auch eine große in Marburg durchgeführte Studie (n=398), welche den Einfluss eines neuen Versorgungsprogrammes bei Typ 2 Diabetikern im Rahmen eines Disease Management Programme (DMP) untersuchte, ergab nebenbefundlich eine große Anzahl an diabeteschen Ehepaaren.

Diese Studienpopulation wurde dann in dieser Dissertation genutzt, um eine mögliche Kausalität des erhöhten T2DM Risikos bei Paaren zu untersuchen.

Die Hypothese lautete daher: "Eine Person mit T2DM ist ursächlich für das erhöhte Risiko seines Partners auch an T2DM zu erkranken".

Um herauszufinden, ob es sich bei dem erhöhten Risiko um eine Kausalität oder eine nicht kausale Ursache handelt, wurden in dieser Arbeit die Bradford Hill Kriterien verwendet. Es wurde versucht jedes Kriterium bei diesem Datensatz anzuwenden und zu prüfen.

Zunächst wurden alle möglichen Paare aus dem großen Datensatz anhand passender Nachnamen und Adressen identifiziert (18 Paare, 36 Einzelpersonen). Diese Personen wurden kontaktiert und zu einem Interview eingeladen, um so viele Informationen wie möglich über das gemeinsame Leben und die T2DM Risikofaktoren zu erlangen.

Nicht alle Paare zeigten sich mit einer erneuten Kontaktaufnahme für ein Interview einverstanden, sodass drei Datensatzgruppen entstanden:

- Interviewte Paare
- Nicht-Interviewte Paare
- Patienten aus der großen Datenbank (unklarer Diabetes-Status der Partner)

Diese drei Gruppen wurden dann untersucht und verglichen um mögliche Unterschiede und Gemeinsamkeiten herauszuarbeiten.

Die Ergebnisse dieser Untersuchung zeigen, dass die genannte Hypothese nicht zutrifft. Es scheint kein kausaler Zusammenhang zwischen einem an T2DM erkrankten Patienten und dem erhöhten Risiko seines Partners auch zu erkranken zu bestehen.

Der Grund für das erhöhte Risiko kann eher durch “assortative mating” erklärt werden. Das bedeutet, dass Menschen mit ähnlichem Lebensumständen (sozioökonomischer Status, Übergewicht und geringer körperlicher Betätigung) häufig untereinander Partner finden.

Zusammenfassend lässt sich sagen, dass ein Partner mit manifestem T2DM ein Risikofaktor, jedoch nicht die auslösende Ursache für ein erhöhtes T2DM-Risiko ist.

## 8 Literature

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## 9 Appendices

### 9.1 Affidavit - Ehrenwörtliche Erklärung

Eine ehrenwörtliche Erklärung über die selbstständige Anfertigung der Dissertation:

Ich erkläre ehrenwörtlich, dass ich die dem Fachbereich Medizin Marburg zur Promotionsprüfung eingereichte Arbeit mit dem Titel *Causation or Assortative Mating: The Social Dynamics in Couples with Both Partners Suffering from the Same Lifestyle Disease. A Case Series Study from a German Cohort Study of Type 2 Diabetes Mellitus Patients in a Disease Management Programme* im Institut für Medizinische Soziologie und Sozialmedizin unter Leitung von Prof. Dr. Dr. Ulrich Mueller mit Unterstützung durch Dr. Andrea Werdecker ohne sonstige Hilfe selbst durchgeführt und bei der Abfassung der Arbeit keine anderen als die in der Dissertation aufgeführten Hilfsmittel benutzt habe. Ich habe bisher an keinem in- oder ausländischen Medizinischen Fachbereich ein Gesuch um Zulassung zur Promotion eingereicht, noch die vorliegende oder eine andere Arbeit als Dissertation vorgelegt.

Ich versichere, dass ich sämtliche wörtlichen oder sinngemäßen Übernahmen und Zitate kenntlich gemacht habe.

Mit dem Einsatz von Software zur Erkennung von Plagiaten bin ich einverstanden.

Ort, Datum, Unterschrift

Die Hinweise zur Erkennung von Plagiaten habe ich zur Kenntnis genommen.

Ort, Datum, Unterschrift Betreuer

## 9.2 Curriculum vitae

### Persönliche Daten:

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Name:	Serge Muttardi
Geburtsdatum:	22.03.1990
Geburtsort:	Düsseldorf
Familienstand:	ledig

### Berufliche Laufbahn:

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Seit April 2017	Arzt in der Weiterbildung im Fachbereich der Inneren Medizin
	- Asklepios Klinik Nord (Prof. Dr. Klaus Herrlinger)

### Akademische Laufbahn:

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2009-2016	Studium der Humanmedizin an der Philipps-Universität Marburg
Mai 2016	3. Ärztliche Prüfung
Oktober 2014	2. Ärztliche Prüfung
September 2011	1. Ärztliche Prüfung

## Dissertation:

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*„Causation or Assortative Mating: The Social Dynamics in Couples with Both Partners Suffering from the Same Lifestyle Disease. A Case Series Study from a German Cohort Study of Type 2 Diabetes Mellitus Patients in a Disease Management Programme“*

in dem Institut für Versorgungsforschung und Klinische Epidemiologie.

(Prof. Dr. Dr. Ulrich Mueller)

## Praktisches Jahr:

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Mai - Sep. 2015	Innere Medizin	Kreiskrankenhaus Frankenberg (Eder)
Sep. - Dez. 2015	Chirurgie	Escuela Osario Danilo Rosales Argüello (HEODRA) in Leon, Nicaragua
Dez. 2015 - April 2016	Anästhesiologie	Asklepios Klinik Heidberg, Hamburg

## Famulaturen:

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März-April 2012	Unfallchirurgie und Orthopädie in der Asklepios Klinik Altona, Hamburg
März-April 2013	Kinder- und Jugendpsychiatrie am Vivantes Klinikum im Friedrichshain, Berlin
Juli-Sep. 2013	Internistische Hausarztpraxis Dr. Weinstock, Düsseldorf (2 Monate)

## **Schul Ausbildung:**

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2006-2008	Oakham School, Rutland (England) Abschluss: International Baccalaureate Note: 1,8
2004-2006	Quirinus-Gymnasium in Neuss
2000-2004	St.-Ursula-Gymnasium in Düsseldorf
1996-2000	Don-Bosco Grundschule in Düsseldorf

## **Sprachkenntnisse:**

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Deutsch:	Muttersprache
Englisch:	fließend
Spanisch:	konversationssicher
Latein:	Latinum

## **Weitere Tätigkeiten und Interessen**

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Interessen:	Sport (Fußball, Handball und weitere), Reisen, Lesen, Kochen
Auslandsaufenthalte:	Nicaragua 2015 (Chirurgisches PJ-Tertial), Verschiedene Sprachkurse (2009-2015 Spanien, Peru und Nicaragua)
Sportliche Tätigkeiten:	Mitglied des Organisationsausschusses der Bunten Liga Marburg (2012-2016)

### 9.3 List of academic teachers

Bartsch, Prof. Dr.	Neubauer, Prof. Dr.
Becker, Prof. Dr.	Neumüller, Prof. Dr.
Bertoune, Dr.	Oertel, Prof. Dr.
Cetin, Prof. Dr.	Oliver, Prof. Dr.
Detsch, PD Dr.	Pagenstecher, Prof. Dr.
Donner-Banzhoff, Prof. Dr.	Pastora, Dr.
Eberhart, Prof. Dr.	Plant, Prof. Dr.
Fendrich, Prof. Dr.	Pryss, Dr.
Feuser	Reese, PD. Dr.
Giese, Prof. Dr.	Renz, Prof. Dr.
Göke, Prof. Dr.	Ruchholtz, Prof. Dr.
Greene, Dr.	Schäfer, Prof. Dr.
Hertl, Prof. Dr.	Schieffer, Prof. Dr.
Hoyer, Prof. Dr.	Schierl, Dr.
Jansen, Prof. Dr.	Seitz, Prof. Dr.
Kann, Prof. Dr. Dr.	Sekundo, Prof. Dr.
Koolmann, Prof. Dr.	Sevinc, Dr.
Lill, Prof. Dr.	Stahl, Prof. Dr.
Lohoff, Prof. Dr.	Vogelmeier, Prof. Dr.
Ludolph, Dr.	Vogt, Prof. Dr.
Mahnken, Prof. Dr.	Wagner, Prof. Dr.
Maier, Prof. Dr.	Werner, Prof. Dr.
Moll, Prof. Dr.	Westermann, Prof. Dr.
Mueller, Prof. Dr. Dr.	Wrocklage, Dr.

## **9.4 Acknowledgements - Danksagung**

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## 9.5 Questionnaire

First I would like to ask some questions about your living together:

1      Since when are you a couple?

Year:

Month:

2      Since when are you living together?

Year:

Month:

2a      Instruction for the interviewer: If couple is married: When did you marry?

Year:

Month:



3. How do you divide the work in the following areas between you two?

If you have a maid or anyone else helping with the household, please refer only to the part of the work taken care of by you two.

3a Washing laundry

- 1- Completely done by the male partner
  - 2- Mostly done by the male partner
  - 3- Roughly even
  - 4- Mostly done by the female partner
  - 5- Completely done by the female partner
  - 6- Only someone else
  - 7- This does not apply to us, because
- 

3b Preparing warm meals

- 1- Completely done by the male partner
  - 2- Mostly done by the male partner
  - 3- Roughly even
  - 4- Mostly done by the female partner
  - 5- Completely done by the female partner
  - 6- Only someone else
  - 7- This does not apply to us, because
- 

3c Preparing cold meals

- 1- Completely done by the male partner

- 2- Mostly done by the male partner
  - 3- Roughly even
  - 4- Mostly done by the female partner
  - 5- Completely done by the female partner
  - 6- Only someone else
  - 7- This does not apply to us, because
- 

3d Grocery shopping

- 1- Completely done by the male partner
  - 2- Mostly done by the male partner
  - 3- Roughly even
  - 4- Mostly done by the female partner
  - 5- Completely done by the female partner
  - 6- Only someone else
  - 7- This does not apply to us, because
- 

3e Financial affairs

- 1- Completely done by the male partner
  - 2- Mostly done by the male partner
  - 3- Roughly even
  - 4- Mostly done by the female partner
  - 5- Completely done by the female partner
  - 6- Only someone else
  - 7- This does not apply to us, because
-

3f Tidying and cleaning the flat/house

- 1- Completely done by the male partner
  - 2- Mostly done by the male partner
  - 3- Roughly even
  - 4- Mostly done by the female partner
  - 5- Completely done by the female partner
  - 6- Only someone else
  - 7- This does not apply to us, because
-

Now I have some questions about your Diabetes illness and the Disease-Management Programm (DMP)

4 Is there a known case of Diabetes type II in your family? Please think about all of your biological relatives, even if they are already deceased.

Male partner	Female partner
No	No

Male partner	Female partner
Yes, namely:	Yes, namely:
Mother	Mother
Father	Father
Grandmother: 1. Paternal 2. Maternal	Grandmother: 1. Paternal 2. Maternal
Grandfather: 1. Paternal 2. Maternal	Grandfather: 1. Paternal 2. Maternal
Uncle (biological)	Uncle (biological)
Aunt (biological)	Aunt (biological)
Number of siblings: Brother(s)	Number of siblings: Brother(s)

Sister(s)	Sister(s)
Children	Children
Children of siblings	Children of siblings
Others:	Others:

5 Since when are you participating in a Disease-Management Programm (DMP), a program for type 2 diabetes patients offered by your health insurance?

Male Partner	Female Partner
Since year:	Since year
Since month	Since month
How satisfied are you so far? (please chose one of the following)	How satisfied are you so far? (please chose one of the following)
Very satisfied	Very satisfied
satisfied	satisfied
Partly satisfied	Partly satisfied
Not satisfied	Not satisfied
Dissatisfied	Dissatisfied

6 a) Have you ever participated in any other training for certain health issues offered by your health insurance, an adult education centre or by any other facility?

Male Partner	Female Partner
No	No
If so	If so
A training for diabetes	A training for diabetes

A training for hypertension Any other training (please name):	A training for hypertension Any other training (please name):
If so- please name your last training	If so- please name your last training
Year	Year
Month	month

b) If you ever participated in such a training, was it your first participation?

<b>Male Partner</b>	<b>Female partner</b>
Yes	Yes
No, I have participated in a training before	No, I have participated in a training before

Do you remember when that was?

<b>Male Partner</b>	<b>Female partner</b>
No	No
Yes,	Yes
Year	Year
Month	Month

7      How was your diabetes mellitus type 2 diagnosed?

Male Partner	Female partner
There have been symptoms and the diabetes was diagnosed in line with the clarification of the symptoms.	There have been symptoms and the diabetes was diagnosed in line with the clarification of the symptoms.
You had a strong suspicion of diabetes – please describe:  _____  —	You had a strong suspicion of diabetes – please describe:  _____  —
Clarification of diabetes upon your own request:  reason: _____  —	Clarification of diabetes upon your own request:  reason: _____  —
By chance due to a routine check-up	By chance due to a routine check-up
Other reasons- please describe  _____  —	Other reasons- please describe  _____  —



8 Has your partner played a role in diagnosing your diabetes- i.e. advising you to consult a doctor, showing you reports about diabetes from the media or anything similar? How was it in your case?

Instruction for the interviewer: write down the answer as literal as possible.

Read out what you have written and ask: "Did I write this down correctly?"

<b>Male Partner</b>	<b>Female partner</b>

9 How does your diabetes treatment look like at the moment- please tick off every suitable answer?

Male Partner	Female partner
Diet	Diet
Insulin	Insulin
_____	_____
—	—
Tablets	Tablets
_____	_____
—	—
other: _____	Other: _____
Male Partner	Female partner
Since when is your diabetes treatment like it is today?	Since when is your diabetes treatment like it is today?
month _____	month _____
year _____	year _____

10 Now we are interested in which exact type of tablets you are taking. Could you show me the pack?

Which dose are you taking every day?

Male Partner	Female partner
<p>Do you remember which treatment you received at the beginning of your diabetes illness? If you took tablets, it is sufficient if you tell me the name (no dosage necessary).</p> <p>no</p>	<p>Do you remember which treatment you received at the beginning of your diabetes illness? If you took tablets, it is sufficient if you tell me the name (no dosage necessary).</p> <p>no</p>
Yes, namely (chose all applicable answers)	Yes, namely (chose all applicable answers)
Diet	Diet
Insulin	Insulin
Tablets	Tablets
Others:_____	Others:_____

12a Have you been diagnosed by any of the following illnesses in the past 6 month? Please chose all applicable answers.

<b>Male Partner</b>	<b>Female partner</b>
Hypertension	Hypertension
Disease of the retina	Disease of the retina
Fat metabolism disorder	Fat metabolism disorder
Kidney disease	Kidney disease
Arterial occlusive disease	Arterial occlusive disease
Atrial fibrillation	Atrial fibrillation
Heart disease	Heart disease
Diabetic foot syndrome	Diabetic foot syndrome

12 b Have any of the following measures been taken in the past 6 month or have any of the following incidents happened to you in the past 6 month?

Please chose all applicable answers.

Male Partner	Female partner
Heart attack	Heart attack
Somatosensory disorder	Somatosensory disorder
Amputation	Amputation
Stroke	Stroke
Blindness	Blindness
Transplantation	Transplantation
Dialysis	Dialysis
Diabetic foot	Diabetic foot
Others:_____	Others:_____

13 Now I would like to know something about your eating and drinking routine.

In the following list, there are different foods and drinks compiled. Please tell me how often you eat or drink each grocery.

**Male partner**

	Several times daily	Daily	Several times weekly	Weekly	1-3 times per month	never
Whole						

grain bread						
White bread, toast						
Fresh fruits						
Fresh or frozen vegetables						
Meat or sausage						
Fried food						
Sweets, cake or other pastry						
Beer or wine						
Hard liquor						

### Female Partner

	Several times daily	Daily	Several times weekly	Weekly	1-3 times per month	never
Whole grain bread						

White bread, toast						
Fresh fruits						
Fresh or frozen vegetables						
Meat or sausage						
Fried food						
Sweets, cake or other pastry						
Beer or wine						
Hard liquor						

14

Have there been phases in your life, in which you have gained or lost much weight? (chose one)	Have there been phases in your life, in which you have gained or lost much weight? (chose one)
Weight was constant	Weight was constant
Weight increased constantly	Weight increased constantly
Weight increased erratically	Weight increased erratically
Weight decreased erratically	Weight decreased erratically
Weight decreased constantly	Weight decreased constantly
Explication: _____ —	Explication: _____ —

15 Now I have some questions about your health situation.

Male Partner	Female partner
<p>When was your height last measured at your doctors practice or elsewhere?</p> <p>Year</p> <p>Month</p> <p>Has never been measured</p> <p>Own measurement</p> <p>I don't know</p>	<p>When was your height last measured at your doctors practice or elsewhere?</p> <p>Year</p> <p>Month</p> <p>Has never been measured</p> <p>Own measurement</p> <p>I don't know</p>
How tall are you _____cm	How tall are you _____cm
How big is your hip size _____cm	How big is your hip size _____cm
(If no data is available): I would now, if it would be possible, measure your hip size.	(If no data is available): I would now, if it would be possible, measure your hip size.
Hip size _____cm	Hip size _____cm
<p>When was your weight last measured at your doctors practice or elsewhere?</p> <p>Has never been measured</p> <p>I don't know</p>	<p>When was your weight last measured at your doctors practice or elsewhere?</p> <p>Has never been measured</p> <p>I don't know</p>
How many kilograms did you weigh? If you don't remember precisely, please	How many kilograms did you weigh? If you don't remember precisely, please



guess: _____ kg	guess: _____ kg
-----------------	-----------------

Now I have some questions about your labour situation.

16 Are you already retired?

**Male partner**

Yes	No

**Male Partner**

Yes	no
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16a If you are retired, have you drawn benefits for reduction in earning capacity or a regular pension at the beginning?

**Male partner**

Benefits for reduction in earning capacity	Regular pension
--	-----------------

**Female partner**

Benefits for reduction in earning capacity	Regular pension
--	-----------------

If you received a Benefits for reduction in earning capacity what was the reason?

**Male partner**

**Female partner**

16bl If you are not yet retired, I would like to know if you are employed or unemployed.

**Male Partner**

Employed	unemployed
----------	------------

**Female Partner**

Employed	unemployed
----------	------------

16bII If you are employed, which employment situation from this list describes yours? (Only one answer possible) Please bear in mind that employment means any paid or with income connected activity.

**Male Partner**

Full-time employed  
Part-time employed  
Marginally employed  
Irregularly employed  
Occupational retraining

**Female Partner**

Full-time employed  
Part-time employed  
Marginally employed  
Irregularly employed  
Occupational retraining